

クロトンアルデヒドのラットを用いた
吸入によるがん原性試験報告書

試験番号 0318

APPENDIX

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(2-YEAR STUDY)
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(2-YEAR STUDY)
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APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILORECTION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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 ANIMAL : RAT F344/DuCrj
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CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTIO | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
|-------------------------|------------|-------------------------|------|------|---|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | | | | | | | | | | | | |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILORECTION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| DEATH | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| PILOERECTION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| DEATH | 0ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 3ppm | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 |
| | 6ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 12ppm | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 5 | 5 | 5 | 5 | 6 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| DEATH | 0ppm | 3 | 3 | 3 | 4 | 6 | 6 |
| | 3ppm | 4 | 5 | 5 | 6 | 6 | 6 |
| | 6ppm | 2 | 4 | 4 | 5 | 5 | 5 |
| | 12ppm | 6 | 6 | 6 | 7 | 7 | 8 |
| MORIBUND SACRIFICE | 0ppm | 3 | 4 | 4 | 4 | 5 | 5 |
| | 3ppm | 2 | 2 | 4 | 4 | 4 | 5 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 4 | 4 | 4 | 4 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 1 | 0 | 0 | 0 | 1 | 0 |
| | 3ppm | 0 | 2 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 2 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 1 | 1 | 1 | 1 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 1 | 0 |
| WASTING | 0ppm | 1 | 0 | 0 | 0 | 1 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | 0ppm | 0 | 0 | 0 | 0 | 1 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 1 | 0 | 0 |
| | 3ppm | 0 | 1 | 0 | 0 | 1 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. EYE | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 2 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 3 | 2 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. EYE | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|---------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 1 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 1 | 1 | 1 | 1 | 2 | 3 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 2 |
| | 6ppm | 2 | 1 | 0 | 0 | 0 | 0 |
| | 12ppm | 2 | 2 | 3 | 1 | 1 | 1 |
| M. NOSE | 0ppm | 0 | 0 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| M. EYE | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 1 | 1 | 1 | 1 | 1 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F944/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | 0ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | 0ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| M. BREAST | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. ANTERIOR. DORSUM | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. BREAST | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| M. ABDOMEN | 0ppm | 2 | 1 | 1 | 1 | 1 | 2 |
| | 3ppm | 1 | 1 | 2 | 2 | 1 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | 0ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| | 3ppm | 2 | 2 | 1 | 1 | 1 | 1 |
| | 6ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 2 | 2 | 1 | 1 | 1 | 1 |
| M. HINDLIMB | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | 0ppm | 1 | 1 | 1 | 1 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. TAIL | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 2 | 1 | 1 | 1 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 2 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 8

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| JAUNDISE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 1 | 0 | 0 | 1 | 1 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| | 12ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 0 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 1 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 2 | 0 | 0 | 0 |

APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| DEATH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| DEATH | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| DEATH | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| DEATH | 0ppm | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| DEATH | 0ppm | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 7 | 7 | 7 |
| | 3ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 3 | 3 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 |
| | 12ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| MORIBUND SACRIFICE | 0ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 3 |
| | 3ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 4 | 5 | 5 | 6 | 6 | 6 | 6 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 |
| | 12ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 4 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| DEATH | 0ppm | 7 | 7 | 8 | 8 | 8 | 8 |
| | 3ppm | 3 | 3 | 3 | 4 | 4 | 4 |
| | 6ppm | 2 | 2 | 2 | 3 | 3 | 3 |
| | 12ppm | 3 | 3 | 3 | 4 | 4 | 4 |
| MORIBUND SACRIFICE | 0ppm | 3 | 3 | 3 | 3 | 3 | 3 |
| | 3ppm | 6 | 6 | 6 | 8 | 8 | 8 |
| | 6ppm | 5 | 5 | 7 | 7 | 7 | 7 |
| | 12ppm | 4 | 4 | 6 | 6 | 6 | 6 |
| LOCOMOTOR MOVEMENT DECR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| HUNCHBACK POSITION | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 1 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 3 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 |
| | 6ppm | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 4 | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| | 6ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 3ppm | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 |
| | 6ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

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ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | | | | | | | | | | | |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 6 | 6 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| | 6ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 |
| | 12ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 1 | 2 | 1 |
| | 12ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 5 | 5 | 5 | 3 | 2 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| SOILED PERI GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE HEMORRHAGIC DISCHA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | 0ppm | 1 | 2 | 2 | 2 | 2 | 2 |
| | 3ppm | 8 | 8 | 8 | 8 | 8 | 8 |
| | 6ppm | 4 | 4 | 4 | 3 | 3 | 3 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | 0ppm | 0 | 0 | 0 | 0 | 1 | 1 |
| | 3ppm | 2 | 1 | 1 | 1 | 1 | 2 |
| | 6ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| | 12ppm | 2 | 2 | 2 | 0 | 0 | 0 |
| M. NOSE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 2 | 2 | 2 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI MOUTH | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 1 | 0 | 0 | 0 | 0 | 0 |

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 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration | | Week-day | | | | | | | | | | | |
|---------------------|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | 0ppm | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| HEMORRHAGE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 6ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M. ABDOMEN | 0ppm | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 |
| | 3ppm | 1 | 2 | 2 | 1 | 1 | 1 | 3 | 3 | 3 | 3 | 2 | 3 | 3 | 3 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| M. POSTERIOR DORSUM | 0ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| ANEMIA | 0ppm | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| | 12ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| HEMORRHAGE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. EAR | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 1 | 1 | 1 | 1 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| M. NECK | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | 0ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 2 | 2 | 2 | 1 | 1 | 1 |
| | 6ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 12ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| M. ABDOMEN | 0ppm | 3 | 3 | 3 | 3 | 3 | 3 |
| | 3ppm | 3 | 3 | 3 | 3 | 3 | 4 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 2 | 2 | 1 | 1 | 1 | 1 |
| M. POSTERIOR DORSUM | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | 0ppm | 0 | 1 | 1 | 1 | 1 | 1 |
| | 3ppm | 2 | 2 | 2 | 1 | 1 | 2 |
| | 6ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| | 12ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 1 | 1 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 2 | 0 | 0 | 1 | 1 |
| | 6ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 59

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 29-7 | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 60

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 61

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 57-7 | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 8

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

PAGE : 62

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 63

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |

(HAN190)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 64

| Clinical sign | Group Name | Administration Week-day | | | | | |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| TORTICOLLIS | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 1 | 0 | 0 | 0 |
| DEEP BREATHING | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA. SOUND | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| SUBNORMAL TEMP | 0ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 12ppm | 0 | 0 | 1 | 0 | 0 | 0 |

APPENDIX B 1

BODY WEIGHT CHANGES: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|---|----------|-----|------|-----|------|------|------|------|------|------|
| | 0-0 | | 1-7 | | 2-7 | | 3-7 | | 4-7 | | 5-7 | |
| 0ppm | 114± | 5 | 142± | 7 | 172± | 9 | 199± | 11 | 222± | 12 | 238± | 13 |
| 3ppm | 114± | 5 | 140± | 7 | 170± | 9 | 195± | 11 | 218± | 12 | 235± | 12 |
| 6ppm | 114± | 5 | 141± | 7 | 171± | 9 | 196± | 10 | 218± | 11 | 236± | 12 |
| 12ppm | 114± | 5 | 137± | 7** | 165± | 9** | 190± | 10** | 211± | 11** | 228± | 12** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|
| | 7-7 | | 8-7 | | 9-7 | | 10-7 | | 11-7 | | 12-7 | |
| 0ppm | 266± | 15 | 278± | 16 | 290± | 17 | 299± | 18 | 305± | 19 | 313± | 19 |
| 3ppm | 262± | 14 | 276± | 15 | 285± | 16 | 294± | 16 | 300± | 17 | 307± | 17 |
| 6ppm | 263± | 15 | 276± | 16 | 287± | 17 | 295± | 17 | 302± | 18 | 309± | 18 |
| 12ppm | 253± | 14** | 263± | 15** | 273± | 16** | 280± | 16** | 285± | 17** | 292± | 17** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|
| | 14-7 | | 18-7 | | 22-7 | | 26-7 | | 30-7 | | 34-7 | |
| 0ppm | 323± | 21 | 340± | 21 | 354± | 24 | 365± | 25 | 376± | 26 | 385± | 27 |
| 3ppm | 317± | 18 | 336± | 20 | 350± | 22 | 363± | 23 | 372± | 24 | 380± | 25 |
| 6ppm | 318± | 18 | 333± | 19 | 346± | 21 | 362± | 21 | 371± | 21 | 380± | 22 |
| 12ppm | 300± | 18** | 314± | 18** | 328± | 20** | 340± | 21** | 348± | 21** | 353± | 21** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 8

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|
| | 42-7 | | 46-7 | | 50-7 | | 54-7 | | 58-7 | | 62-7 | |
| 0ppm | 398± | 29 | 404± | 29 | 409± | 30 | 409± | 30 | 414± | 30 | 419± | 30 |
| 3ppm | 397± | 28 | 403± | 28 | 408± | 29 | 411± | 28 | 417± | 29 | 420± | 29 |
| 6ppm | 392± | 23 | 397± | 23 | 401± | 23 | 405± | 23 | 409± | 25 | 412± | 26 |
| 12ppm | 365± | 21** | 372± | 21** | 376± | 21** | 379± | 21** | 382± | 23** | 387± | 23** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 5

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|
| | 70-7 | | 74-7 | | 78-7 | | 82-7 | | 86-7 | | 90-7 | |
| 0ppm | 424± | 31 | 424± | 33 | 423± | 35 | 421± | 38 | 420± | 37 | 414± | 45 |
| 3ppm | 423± | 30 | 424± | 32 | 424± | 35 | 424± | 36 | 424± | 35 | 421± | 36 |
| 6ppm | 417± | 26 | 418± | 27 | 418± | 28 | 417± | 29 | 413± | 29 | 412± | 30 |
| 12ppm | 391± | 29** | 394± | 36** | 392± | 24** | 388± | 32** | 387± | 25** | 384± | 26** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 6

| Group Name | Administration week-day | | | | | |
|------------|-------------------------|------|-------|------|-------|------|
| | 98-7 | | 102-7 | | 104-7 | |
| 0ppm | 404± | 54 | 403± | 56 | 405± | 50 |
| 3ppm | 409± | 43 | 407± | 36 | 401± | 38 |
| 6ppm | 400± | 31 | 395± | 30 | 388± | 31 |
| 12ppm | 376± | 29** | 373± | 31** | 369± | 32** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 7

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|---|----------|---|------|----|------|-----|------|-----|------|-----|
| | 0-0 | | 1-7 | | 2-7 | | 3-7 | | 4-7 | | 5-7 | |
| 0ppm | 94± | 3 | 108± | 5 | 121± | 6 | 133± | 6 | 140± | 7 | 148± | 8 |
| 3ppm | 94± | 3 | 108± | 4 | 121± | 5 | 131± | 6 | 140± | 7 | 147± | 7 |
| 6ppm | 94± | 3 | 109± | 4 | 121± | 4 | 132± | 6 | 139± | 6 | 146± | 7 |
| 12ppm | 94± | 3 | 107± | 4 | 118± | 5* | 128± | 5** | 135± | 6** | 142± | 7** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 8

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 8

| Group Name | Administration week-day | | 7-7 | | 8-7 | | 9-7 | | 10-7 | | 11-7 | | 12-7 | | 13-7 | |
|---|-------------------------|-----|------|-----|------|------|------|------|------|------|------|------|------|------|------|--|
| | | | | | | | | | | | | | | | | |
| 0ppm | 158± | 8 | 162± | 10 | 167± | 10 | 172± | 10 | 175± | 10 | 178± | 10 | 183± | 11 | | |
| 3ppm | 157± | 8 | 162± | 8 | 167± | 9 | 171± | 9 | 174± | 9 | 176± | 9 | 181± | 10 | | |
| 6ppm | 155± | 9 | 159± | 9 | 164± | 10 | 168± | 10 | 171± | 10 | 173± | 10* | 177± | 11* | | |
| 12ppm | 151± | 8** | 155± | 9** | 159± | 10** | 163± | 10** | 166± | 10** | 168± | 10** | 172± | 10** | | |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | | | | | | | | | | |

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 9

| Group Name | Administration week-day | | | | | | | | | | | |
|------------|-------------------------|------|------|-----|------|------|------|------|------|------|------|------|
| | 14-7 | | 18-7 | | 22-7 | | 26-7 | | 30-7 | | 34-7 | |
| 0ppm | 181± | 10 | 190± | 11 | 193± | 12 | 201± | 13 | 203± | 13 | 207± | 14 |
| 3ppm | 181± | 10 | 188± | 10 | 192± | 10 | 199± | 11 | 202± | 11 | 207± | 11 |
| 6ppm | 176± | 10* | 184± | 10* | 190± | 11 | 196± | 13 | 200± | 13 | 205± | 12 |
| 12ppm | 172± | 10** | 177± | 9** | 182± | 10** | 187± | 10** | 191± | 11** | 193± | 10** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 10

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|
| | 42-7 | | 46-7 | | 50-7 | | 54-7 | | 58-7 | | 62-7 | |
| 0ppm | 217± | 15 | 219± | 15 | 224± | 15 | 227± | 17 | 232± | 18 | 236± | 18 |
| 3ppm | 215± | 12 | 218± | 13 | 223± | 14 | 225± | 14 | 230± | 15 | 234± | 20 |
| 6ppm | 214± | 14 | 218± | 14 | 224± | 14 | 228± | 15 | 231± | 16 | 237± | 16 |
| 12ppm | 202± | 13** | 206± | 13** | 211± | 14** | 215± | 14** | 215± | 14** | 222± | 15** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 11

| Group Name | Administration | | week-day | | | | | | | | | |
|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|
| | 70-7 | | 74-7 | | 78-7 | | 82-7 | | 86-7 | | 90-7 | |
| 0ppm | 246± | 19 | 252± | 20 | 257± | 20 | 262± | 21 | 262± | 22 | 266± | 23 |
| 3ppm | 245± | 20 | 250± | 21 | 255± | 20 | 259± | 20 | 261± | 21 | 264± | 24 |
| 6ppm | 247± | 20 | 251± | 21 | 255± | 21 | 260± | 22 | 263± | 23 | 264± | 31 |
| 12ppm | 227± | 16** | 231± | 17** | 235± | 17** | 238± | 18** | 239± | 19** | 242± | 19** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 12

| Group Name | Administration week-day | | | | | |
|------------|-------------------------|------|-------|------|-------|------|
| | 98-7 | | 102-7 | | 104-7 | |
| 0ppm | 269± | 28 | 275± | 23 | 272± | 24 |
| 3ppm | 268± | 20 | 272± | 20 | 272± | 20 |
| 6ppm | 268± | 26 | 270± | 21 | 269± | 21 |
| 12ppm | 245± | 26** | 250± | 19** | 248± | 21** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(HAN260)

BAIS 3

APPENDIX C 1

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

| Group Name | Administration week-day(effective) | | | | | | |
|------------|------------------------------------|-------------|-------------|-----------|-----------|-----------|-------------|
| | 1-7 (6) | 2-7 (7) | 3-7 (7) | 4-7 (7) | 5-7 (7) | 6-7 (7) | 7-7 (7) |
| 0ppm | 14.5± 1.1 | 15.5± 1.1 | 16.9± 1.2 | 17.3± 1.2 | 17.3± 1.1 | 16.7± 1.0 | 16.9± 1.0 |
| 3ppm | 14.1± 0.8 | 15.3± 1.1 | 16.7± 1.2 | 17.2± 1.2 | 17.1± 1.1 | 16.4± 0.9 | 16.7± 1.1 |
| 6ppm | 14.3± 1.0 | 15.4± 0.9 | 16.4± 1.0 | 17.2± 1.0 | 17.2± 1.1 | 16.8± 1.1 | 16.5± 1.3 |
| 12ppm | 13.6± 1.0** | 14.9± 1.1** | 16.0± 1.2** | 16.9± 1.1 | 17.0± 1.3 | 16.3± 1.1 | 16.1± 1.1** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

| Group Name | Administration week-day(effective) | | | | | | |
|------------|------------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| | 8-7(7) | 9-7(7) | 10-7(7) | 11-7(7) | 12-7(7) | 13-7(7) | 14-7(7) |
| 0ppm | 16.9± 1.1 | 17.2± 1.2 | 17.5± 1.1 | 16.9± 1.1 | 16.8± 1.1 | 17.4± 1.3 | 16.7± 1.2 |
| 3ppm | 16.5± 1.1 | 16.5± 1.3** | 16.9± 1.1* | 16.4± 1.2 | 16.3± 1.1* | 16.9± 1.3 | 16.5± 1.1 |
| 6ppm | 16.9± 1.2 | 16.7± 1.0 | 17.2± 1.2 | 16.5± 1.1 | 16.7± 1.0 | 17.3± 1.2 | 16.3± 0.9 |
| 12ppm | 16.2± 1.1** | 16.0± 1.1** | 16.5± 1.1** | 16.0± 1.0** | 16.0± 1.0** | 16.5± 1.3** | 15.5± 1.0** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 8

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

| Group Name | Administration week-day(effective) | | | | | | |
|------------|------------------------------------|------------|-------------|-------------|-------------|------------|-----------|
| | 18-7(7) | 22-7(7) | 26-7(7) | 30-7(7) | 34-7(7) | 38-7(7) | 42-7(7) |
| 0ppm | 16.8± 1.1 | 16.9± 1.3 | 16.8± 1.4 | 17.0± 1.1 | 17.1± 1.3 | 17.0± 1.3 | 16.9± 1.4 |
| 3ppm | 16.5± 1.2 | 16.7± 1.3 | 17.0± 0.9 | 16.8± 1.3 | 17.1± 1.2 | 17.1± 1.2 | 17.0± 1.3 |
| 6ppm | 16.2± 1.0** | 16.9± 1.2 | 17.7± 1.3** | 17.0± 1.0 | 17.2± 1.1 | 17.0± 0.9 | 17.2± 1.2 |
| 12ppm | 16.2± 0.9** | 16.3± 1.0* | 16.6± 1.1 | 16.3± 1.0** | 16.4± 1.0** | 16.4± 1.0* | 16.6± 0.8 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

| Group Name | Administration week-day(effective) | | | | | | |
|------------|------------------------------------|-------------|-----------|-------------|-----------|-----------|-------------|
| | 46-7(7) | 50-7(7) | 54-7(7) | 58-7(7) | 62-7(7) | 66-7(7) | 70-7(7) |
| 0ppm | 16.9± 1.3 | 17.7± 1.3 | 17.3± 1.2 | 17.7± 1.1 | 17.6± 1.3 | 17.3± 1.2 | 17.3± 1.1 |
| 3ppm | 17.1± 1.1 | 17.3± 1.3 | 17.4± 1.0 | 17.8± 1.2 | 17.6± 1.2 | 17.3± 1.2 | 17.5± 1.2 |
| 6ppm | 17.1± 1.1 | 17.3± 1.1 | 17.7± 1.1 | 17.6± 1.1 | 17.7± 1.5 | 17.5± 1.2 | 16.9± 1.3 |
| 12ppm | 16.8± 1.1 | 16.9± 0.9** | 17.2± 1.0 | 16.9± 1.1** | 17.2± 1.0 | 16.7± 1.0 | 16.2± 1.3** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 5

| Group Name | Administration | | week-day(effective) | | | | | | | | | | | |
|------------|----------------|-----|---------------------|------|---------|-------|---------|-----|---------|-----|---------|-----|---------|-----|
| | 74-7(7) | | 78-7(7) | | 82-7(7) | | 86-7(7) | | 90-7(7) | | 94-7(7) | | 98-7(7) | |
| 0ppm | 17.4± | 1.6 | 17.6± | 1.3 | 17.2± | 1.3 | 17.3± | 1.4 | 16.9± | 2.0 | 16.6± | 1.4 | 16.5± | 2.2 |
| 3ppm | 17.7± | 1.5 | 17.3± | 2.1 | 16.9± | 2.0 | 17.3± | 1.5 | 17.6± | 1.8 | 16.8± | 1.4 | 16.5± | 3.4 |
| 6ppm | 17.3± | 1.2 | 17.6± | 1.4 | 16.7± | 1.7 | 17.1± | 1.1 | 17.3± | 1.3 | 16.8± | 1.8 | 16.6± | 1.7 |
| 12ppm | 17.2± | 2.0 | 17.1± | 1.5* | 15.9± | 2.5** | 16.7± | 1.1 | 16.8± | 1.0 | 16.0± | 1.4 | 16.2± | 1.5 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 6

| Group Name | Administration week-day(effective) | |
|------------|------------------------------------|-----------|
| | 102-7(7) | 104-7(7) |
| 0ppm | 16.5± 2.4 | 17.2± 2.1 |
| 3ppm | 16.8± 1.8 | 17.2± 2.6 |
| 6ppm | 17.3± 1.8 | 17.2± 1.9 |
| 12ppm | 16.6± 1.4 | 17.2± 1.4 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 8

APPENDIX C 2

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 7

| Group Name | Administration 1-7 (6) | week-day(effective) 2-7 (7) | 3-7 (7) | 4-7 (7) | 5-7 (7) | 6-7 (7) | 7-7 (7) |
|------------|---------------------------|--------------------------------|-------------|-----------|-------------|-------------|-----------|
| 0ppm | 10.8± 0.8 | 11.0± 0.7 | 11.6± 0.6 | 11.6± 0.8 | 11.8± 1.1 | 11.4± 0.8 | 11.3± 1.0 |
| 3ppm | 10.6± 0.6 | 11.0± 0.6 | 11.4± 0.8 | 11.6± 0.7 | 11.5± 0.8 | 11.3± 1.1 | 11.0± 1.0 |
| 6ppm | 10.7± 0.6 | 10.8± 0.6 | 11.4± 0.8 | 11.4± 0.8 | 11.6± 1.0 | 10.9± 0.8* | 10.9± 0.9 |
| 12ppm | 10.4± 0.7 | 10.7± 0.5* | 11.0± 1.0** | 11.4± 0.6 | 11.1± 0.7** | 10.8± 0.9** | 10.9± 1.0 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 8

| Group Name | Administration week-day(effective) | | | | | | |
|---|------------------------------------|-----------|-------------|------------|-------------|-----------|-------------|
| | 8-7(7) | 9-7(7) | 10-7(7) | 11-7(7) | 12-7(7) | 13-7(7) | 14-7(7) |
| 0ppm | 11.2± 1.0 | 11.3± 0.9 | 11.6± 0.8 | 11.7± 1.1 | 11.5± 0.9 | 12.5± 1.5 | 11.4± 1.5 |
| 3ppm | 11.0± 1.1 | 11.3± 1.0 | 11.1± 1.0* | 11.4± 1.0 | 11.3± 0.9 | 12.0± 1.6 | 11.3± 1.2 |
| 6ppm | 10.5± 0.8** | 11.4± 1.0 | 10.8± 0.8** | 11.1± 1.0* | 10.8± 0.9** | 12.2± 1.4 | 10.3± 1.0** |
| 12ppm | 10.5± 0.9** | 11.1± 1.4 | 10.8± 0.8** | 11.3± 1.1 | 10.5± 0.6** | 12.5± 1.6 | 10.3± 0.7** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 9

| Group Name | Administration 18-7(7) | week-day(effective) 22-7(7) | 26-7(7) | 30-7(7) | 34-7(7) | 38-7(7) | 42-7(7) |
|------------|---------------------------|--------------------------------|-------------|-----------|-------------|-------------|-----------|
| 0ppm | 11.5± 1.3 | 11.5± 1.0 | 11.9± 1.6 | 11.1± 1.1 | 11.6± 1.6 | 11.7± 1.1 | 11.5± 1.1 |
| 3ppm | 11.2± 1.1 | 11.5± 1.2 | 11.3± 1.4 | 11.3± 0.9 | 12.0± 1.1 | 11.3± 1.0* | 11.5± 1.0 |
| 6ppm | 10.9± 0.9* | 11.3± 1.0 | 11.1± 1.0* | 11.2± 0.9 | 11.3± 1.0 | 11.3± 0.8 | 11.1± 0.9 |
| 12ppm | 10.9± 0.8* | 10.9± 0.8* | 10.7± 0.7** | 11.0± 0.8 | 10.8± 0.8** | 10.6± 0.8** | 11.1± 1.0 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 10

| Group Name | Administration 46-7(7) | week-day(effective) 50-7(7) | 54-7(7) | 58-7(7) | 62-7(7) | 66-7(7) | 70-7(7) |
|---|---------------------------|--------------------------------|-----------|-------------|-----------|-----------|-------------|
| 0ppm | 11.3± 0.8 | 12.1± 1.1 | 11.8± 1.0 | 12.6± 1.2 | 12.1± 1.1 | 11.6± 0.8 | 12.3± 1.1 |
| 3ppm | 11.3± 1.0 | 11.8± 1.0 | 11.6± 1.0 | 12.3± 1.0 | 12.1± 2.0 | 11.9± 1.1 | 12.3± 1.0 |
| 6ppm | 11.3± 0.9 | 11.6± 0.9* | 11.8± 0.9 | 11.7± 0.9** | 12.2± 0.8 | 11.6± 0.8 | 11.9± 0.9 |
| 12ppm | 11.1± 1.0 | 11.6± 1.2* | 11.4± 0.9 | 11.3± 0.8** | 11.7± 0.9 | 11.2± 0.7 | 11.5± 1.1** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |

(HAN260)

BAIS 8

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 11

| Group Name | Administration week-day(effective) | | | | | | |
|------------|------------------------------------|-----------|-------------|------------|-----------|-----------|-----------|
| | 74-7(7) | 78-7(7) | 82-7(7) | 86-7(7) | 90-7(7) | 94-7(7) | 98-7(7) |
| 0ppm | 12.4± 1.0 | 12.5± 1.0 | 12.6± 1.2 | 12.2± 1.4 | 12.6± 1.1 | 11.7± 1.8 | 12.5± 2.3 |
| 3ppm | 12.4± 1.0 | 12.5± 0.8 | 12.7± 1.0 | 12.6± 1.0 | 12.6± 1.4 | 12.0± 1.5 | 12.8± 1.1 |
| 6ppm | 12.5± 1.6 | 12.3± 0.9 | 12.4± 0.8 | 12.6± 0.9 | 12.2± 1.8 | 12.1± 1.4 | 12.7± 2.0 |
| 12ppm | 11.9± 0.9* | 12.2± 0.8 | 11.4± 1.1** | 11.7± 0.9* | 12.3± 0.8 | 11.6± 1.6 | 12.0± 2.1 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 12

| Group Name | Administration week-day(effective) | |
|------------|------------------------------------|-----------|
| | 102-7(7) | 104-7(7) |
| 0ppm | 12.7± 1.0 | 12.4± 1.8 |
| 3ppm | 12.7± 1.2 | 12.9± 1.3 |
| 6ppm | 12.7± 1.5 | 12.7± 0.9 |
| 12ppm | 12.1± 0.9* | 12.1± 1.2 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 8

APPENDIX D 1

HEMATOLOGY: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 1

| Group Name | NO. of Animals | RED BLOOD CELL 10 ⁶ /μl | | HEMOGLOBIN g/dl | | HEMATOCRIT % | | MCV fl | | MCH pg | | MCHC g/dl | | PLATELET 10 ³ /μl | |
|------------|-------------------|---------------------------------------|------|--------------------|-----|-----------------|-----|-----------|-----|-----------|-----|--------------|-----|---------------------------------|-----|
| 0ppm | 38 | 8.28± | 1.39 | 13.8± | 2.5 | 42.4± | 6.4 | 51.5± | 3.6 | 16.6± | 1.4 | 32.3± | 1.5 | 993± | 255 |
| 3ppm | 39 | 8.05± | 1.81 | 13.5± | 3.1 | 41.4± | 8.1 | 52.6± | 7.9 | 16.9± | 2.0 | 32.3± | 1.9 | 1002± | 321 |
| 6ppm | 45 | 8.36± | 1.34 | 13.8± | 2.6 | 42.3± | 6.7 | 50.8± | 3.3 | 16.5± | 1.3 | 32.4± | 1.6 | 948± | 289 |
| 12ppm | 38 | 8.25± | 1.68 | 13.5± | 3.0 | 41.7± | 7.6 | 51.1± | 5.3 | 16.4± | 1.7 | 32.2± | 1.8 | 972± | 235 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of Animals | WBC 1 O ³ /μl | | Differential N-BAND | | WBC (%) N-SEG | | EOSINO | | BASO | | MONO | | LYMPHO | | OTHER | |
|------------|-------------------|-----------------------------|-------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|-------|----|
| 0ppm | 38 | 12.33± | 32.83 | 1± | 1 | 48± | 12 | 1± | 1 | 0± | 0 | 5± | 3 | 41± | 11 | 4± | 15 |
| 3ppm | 39 | 7.06± | 3.33 | 1± | 1 | 49± | 9 | 1± | 1 | 0± | 0 | 4± | 3 | 41± | 11 | 5± | 13 |
| 6ppm | 45 | 7.08± | 3.15 | 1± | 1 | 51± | 11 | 1± | 1 | 0± | 0 | 3± | 2 | 41± | 8 | 2± | 8 |
| 12ppm | 38 | 8.21± | 3.93 | 1± | 1 | 48± | 11 | 1± | 1 | 0± | 0 | 4± | 2 | 41± | 9 | 5± | 11 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

APPENDIX D 2

HEMATOLOGY: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 3

| Group Name | NO. of Animals | RED BLOOD CELL 10 ⁶ /μl | | HEMOGLOBIN g/dl | | HEMATOCRIT % | | MCV fl | | MCH pg | | MCHC g/dl | | PLATELET 10 ³ /μl | |
|------------|-------------------|---------------------------------------|------|--------------------|-----|-----------------|-----|-----------|-----|-----------|-----|--------------|-----|---------------------------------|-----|
| 0ppm | 39 | 8.27± | 0.65 | 14.9± | 1.3 | 44.0± | 3.1 | 53.2± | 2.0 | 18.1± | 0.8 | 33.9± | 0.9 | 643± | 100 |
| 3ppm | 38 | 8.12± | 1.07 | 14.8± | 1.6 | 43.6± | 3.9 | 54.1± | 4.6 | 18.3± | 1.1 | 34.0± | 1.0 | 600± | 141 |
| 6ppm | 39 | 8.27± | 1.21 | 15.0± | 2.3 | 44.1± | 5.7 | 53.8± | 4.3 | 18.1± | 0.8 | 33.7± | 2.0 | 654± | 113 |
| 12ppm | 39 | 8.51± | 0.58 | 15.4± | 1.0 | 45.2± | 2.5 | 53.2± | 1.6 | 18.2± | 0.5 | 34.2± | 0.6 | 644± | 74 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of Animals | WBC 10 ³ /μl | | Differential N-BAND | | WBC (%) N-SEG | | EOSINO | | BASO | | MONO | | LYMPHO | | OTHER | |
|------------|-------------------|----------------------------|------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|-------|----|
| 0ppm | 39 | 5.13± | 6.40 | 1± | 1 | 44± | 13 | 2± | 1 | 0± | 0 | 3± | 2 | 48± | 13 | 2± | 4 |
| 3ppm | 38 | 5.39± | 8.96 | 1± | 1 | 42± | 14 | 1± | 1 | 0± | 0 | 3± | 2 | 48± | 14 | 4± | 13 |
| 6ppm | 39 | 3.57± | 1.28 | 1± | 2 | 46± | 9 | 1± | 1 | 0± | 0 | 4± | 2 | 46± | 10 | 2± | 3 |
| 12ppm | 39 | 3.38± | 1.23 | 1± | 1 | 41± | 8 | 1± | 1 | 0± | 0 | 4± | 2 | 52± | 9 | 1± | 1 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

APPENDIX E 1

BIOCHEMISTRY: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 1

| Group Name | NO. of Animals | TOTAL PROTEIN g/dl | | ALBUMIN g/dl | | A/G RATIO | | T-BILIRUBIN mg/dl | | GLUCOSE mg/dl | | T-CHOLESTEROL mg/dl | | TRIGLYCERIDE mg/dl | |
|------------|-------------------|-----------------------|-----|-----------------|-----|-----------|-----|----------------------|------|------------------|----|------------------------|----|-----------------------|------|
| 0ppm | 38 | 6.5± | 0.3 | 3.3± | 0.2 | 1.1± | 0.1 | 0.17± | 0.05 | 150± | 18 | 178± | 56 | 105± | 63 |
| 3ppm | 39 | 6.5± | 0.4 | 3.3± | 0.3 | 1.1± | 0.2 | 0.20± | 0.23 | 146± | 24 | 195± | 72 | 122± | 108 |
| 6ppm | 45 | 6.5± | 0.5 | 3.3± | 0.3 | 1.0± | 0.1 | 0.16± | 0.07 | 136± | 24 | 174± | 59 | 99± | 79 |
| 12ppm | 38 | 6.5± | 0.3 | 3.3± | 0.2 | 1.0± | 0.1 | 0.16± | 0.04 | 144± | 16 | 154± | 50 | 62± | 53** |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of Animals | PHOSPHOLIPID mg/dl | | GOT IU/l | | GPT IU/l | | LDH IU/l | | ALP IU/l | | G-GTP IU/l | | CPK IU/l | |
|------------|-------------------|-----------------------|-----|-------------|-----|-------------|-----|-------------|-----|-------------|-----|---------------|---|-------------|-----|
| 0ppm | 38 | 260± | 71 | 81± | 58 | 36± | 10 | 185± | 85 | 207± | 86 | 11± | 6 | 86± | 20 |
| 3ppm | 39 | 286± | 105 | 94± | 131 | 39± | 21 | 203± | 109 | 189± | 60 | 10± | 6 | 86± | 21 |
| 6ppm | 45 | 257± | 88 | 86± | 63 | 48± | 59 | 221± | 216 | 222± | 224 | 10± | 7 | 162± | 353 |
| 12ppm | 38 | 233± | 65 | 155± | 384 | 62± | 116 | 209± | 254 | 242± | 125 | 12± | 8 | 88± | 20 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 3

| Group Name | NO. of Animals | UREA NITROGEN mg/dl | | CREATININE mg/dl | | SODIUM mEq/l | | POTASSIUM mEq/l | | CHLORIDE mEq/l | | CALCIUM mg/dl | | INORGANIC PHOSPHORUS mg/dl | |
|------------|-------------------|------------------------|------|---------------------|-----|-----------------|---|--------------------|-----|-------------------|---|------------------|-----|-------------------------------|-----|
| 0ppm | 38 | 20.3± | 3.4 | 0.6± | 0.1 | 141± | 2 | 4.0± | 0.4 | 105± | 2 | 10.4± | 0.3 | 4.2± | 0.6 |
| 3ppm | 39 | 20.5± | 7.3 | 0.6± | 0.2 | 141± | 1 | 3.9± | 0.3 | 105± | 2 | 10.7± | 1.2 | 4.2± | 1.0 |
| 6ppm | 45 | 22.6± | 10.8 | 0.6± | 0.1 | 141± | 2 | 3.9± | 0.3 | 105± | 3 | 10.4± | 0.4 | 4.4± | 1.0 |
| 12ppm | 38 | 20.3± | 3.3 | 0.6± | 0.1 | 140± | 1 | 4.0± | 0.3 | 105± | 1 | 10.3± | 0.3 | 4.4± | 0.6 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

APPENDIX E 2

BIOCHEMISTRY: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of Animals | TOTAL PROTEIN g/dl | | ALBUMIN g/dl | | A/G RATIO | | T-BILIRUBIN mg/dl | | GLUCOSE mg/dl | | T-CHOLESTEROL mg/dl | | TRIGLYCERIDE mg/dl | |
|------------|-------------------|-----------------------|-----|-----------------|-----|-----------|-----|----------------------|------|------------------|----|------------------------|----|-----------------------|------|
| 0ppm | 39 | 6.8± | 0.4 | 4.0± | 0.4 | 1.4± | 0.2 | 0.15± | 0.05 | 137± | 17 | 121± | 33 | 71± | 70 |
| 3ppm | 38 | 6.8± | 0.4 | 4.1± | 0.3 | 1.5± | 0.2 | 0.15± | 0.05 | 141± | 14 | 122± | 26 | 49± | 31 |
| 6ppm | 39 | 6.8± | 0.4 | 4.0± | 0.3 | 1.5± | 0.2 | 0.17± | 0.18 | 136± | 23 | 120± | 28 | 54± | 41 |
| 12ppm | 39 | 6.7± | 0.4 | 4.0± | 0.3 | 1.5± | 0.1 | 0.15± | 0.03 | 140± | 14 | 116± | 19 | 34± | 15** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 5

| Group Name | NO. of Animals | PHOSPHOLIPID mg/dl | | GOT IU/l | | GPT IU/l | | LDH IU/l | | ALP IU/l | | G-GTP IU/l | | CPK IU/l | |
|------------|-------------------|-----------------------|----|-------------|-----|-------------|----|-------------|----|-------------|-----|---------------|---|-------------|----|
| 0ppm | 39 | 226± | 58 | 134± | 91 | 65± | 23 | 202± | 89 | 175± | 204 | 5± | 3 | 89± | 79 |
| 3ppm | 38 | 221± | 45 | 145± | 69 | 69± | 24 | 238± | 84 | 138± | 63 | 5± | 4 | 89± | 33 |
| 6ppm | 39 | 225± | 48 | 159± | 131 | 77± | 39 | 233± | 98 | 159± | 115 | 6± | 6 | 91± | 65 |
| 12ppm | 39 | 212± | 33 | 138± | 117 | 67± | 39 | 206± | 56 | 142± | 53 | 5± | 2 | 77± | 11 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 6

| Group Name | NO. of Animals | UREA NITROGEN mg/dl | | CREATININE mg/dl | | SODIUM mEq/l | | POTASSIUM mEq/l | | CHLORIDE mEq/l | | CALCIUM mg/dl | | INORGANIC PHOSPHORUS mg/dl | |
|------------|-------------------|------------------------|------|---------------------|-----|-----------------|---|--------------------|-----|-------------------|---|------------------|-----|-------------------------------|-----|
| 0ppm | 39 | 20.4± | 18.4 | 0.6± | 0.3 | 140± | 2 | 3.8± | 0.5 | 103± | 3 | 10.3± | 0.3 | 3.9± | 1.5 |
| 3ppm | 38 | 18.6± | 2.6 | 0.5± | 0.1 | 140± | 2 | 3.7± | 0.4 | 104± | 2 | 10.4± | 0.4 | 3.9± | 0.8 |
| 6ppm | 39 | 18.2± | 2.0 | 0.5± | 0.0 | 140± | 2 | 3.7± | 0.4 | 103± | 2 | 10.3± | 0.3 | 4.0± | 0.8 |
| 12ppm | 39 | 18.8± | 1.7 | 0.5± | 0.1 | 140± | 2 | 3.7± | 0.4 | 104± | 2 | 10.3± | 0.3 | 3.9± | 0.8 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

APPENDIX F 1

URINALYSIS: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 1

| Group Name | NO. of Animals | pH | | | | | | | CHI | Protein | | | | | CHI | Glucose | | | | | CHI | Ketone body | | | | | CHI | Bilirubin | | | CHI | | | |
|------------|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|---|---|----|----|-----|---------|----|---|---|----|-----|-------------|----|----|---|---|-----|-----------|----|----|-----|---|---|----|
| | | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | | - | ± | + | 2+ | 3+ | | 4+ | - | ± | + | 2+ | | 3+ | 4+ | - | ± | + | | 2+ | 3+ | 4+ | | - | + | 2+ |
| 0ppm | 41 | 0 | 2 | 7 | 6 | 23 | 3 | 0 | | 0 | 0 | 1 | 6 | 14 | 20 | | 41 | 0 | 0 | 0 | 0 | 0 | | 41 | 0 | 0 | 0 | 0 | 0 | | 40 | 1 | 0 | 0 |
| 3ppm | 40 | 0 | 1 | 5 | 9 | 20 | 5 | 0 | | 0 | 0 | 1 | 0 | 16 | 23 | | 40 | 0 | 0 | 0 | 0 | 0 | | 40 | 0 | 0 | 0 | 0 | 0 | | 38 | 1 | 0 | 1 |
| 6ppm | 45 | 0 | 2 | 7 | 7 | 27 | 2 | 0 | | 0 | 0 | 0 | 5 | 10 | 30 | | 45 | 0 | 0 | 0 | 0 | 0 | | 44 | 1 | 0 | 0 | 0 | 0 | | 45 | 0 | 0 | 0 |
| 12ppm | 39 | 0 | 1 | 3 | 10 | 21 | 3 | 1 | | 0 | 0 | 0 | 3 | 18 | 18 | | 39 | 0 | 0 | 0 | 0 | 0 | | 39 | 0 | 0 | 0 | 0 | 0 | | 39 | 0 | 0 | 0 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of Animals | Occult blood | | | | | CHI | Urobilinogen | | | | | CHI |
|------------|-------------------|--------------|---|---|----|----|-----|--------------|---|----|----|----|-----|
| | | - | ± | + | 2+ | 3+ | | ± | + | 2+ | 3+ | 4+ | |
| 0ppm | 41 | 41 | 0 | 0 | 0 | 0 | 0 | 41 | 0 | 0 | 0 | 0 | 0 |
| 3ppm | 40 | 37 | 2 | 0 | 0 | 0 | 1 | 40 | 0 | 0 | 0 | 0 | 0 |
| 6ppm | 45 | 41 | 0 | 1 | 2 | 1 | 1 | 45 | 0 | 0 | 0 | 0 | 0 |
| 12ppm | 39 | 38 | 0 | 0 | 0 | 0 | 1 | 39 | 0 | 0 | 0 | 0 | 0 |

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3

APPENDIX F 2

URINALYSIS: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 3

| Group Name | NO. of Animals | pH | | | | | | | CHI | Protein | | | | | | CHI | Glucose | | | | | | CHI | Ketone body | | | | | | CHI | Bilirubin | | | | CHI |
|------------|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|---|----|----|----|----|-----|---------|---|---|----|----|----|-----|-------------|----|---|----|----|----|-----|-----------|---|----|----|-----|
| | | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | | - | ± | + | 2+ | 3+ | 4+ | | - | ± | + | 2+ | 3+ | 4+ | | - | ± | + | 2+ | 3+ | 4+ | | - | + | 2+ | 3+ | |
| 0ppm | 39 | 0 | 0 | 2 | 7 | 18 | 12 | 0 | | 0 | 7 | 7 | 12 | 12 | 1 | | 39 | 0 | 0 | 0 | 0 | 0 | | 29 | 9 | 1 | 0 | 0 | 0 | | 39 | 0 | 0 | 0 | |
| 3ppm | 38 | 0 | 0 | 3 | 4 | 11 | 18 | 2 | | 0 | 7 | 10 | 11 | 6 | 4 | | 38 | 0 | 0 | 0 | 0 | 0 | | 29 | 8 | 1 | 0 | 0 | 0 | | 38 | 0 | 0 | 0 | |
| 6ppm | 40 | 0 | 0 | 2 | 4 | 8 | 22 | 4 | * | 0 | 2 | 12 | 12 | 11 | 3 | | 40 | 0 | 0 | 0 | 0 | 0 | | 27 | 13 | 0 | 0 | 0 | 0 | | 39 | 1 | 0 | 0 | |
| 12ppm | 40 | 0 | 0 | 1 | 7 | 4 | 21 | 7 | ** | 0 | 3 | 17 | 14 | 4 | 2 | * | 40 | 0 | 0 | 0 | 0 | 0 | | 29 | 11 | 0 | 0 | 0 | 0 | | 40 | 0 | 0 | 0 | |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of Animals | Occult blood | | | | | Urobilinogen | | | | | | |
|------------|-------------------|--------------|---|---|----|----|--------------|----|---|----|----|----|-----|
| | | - | ± | + | 2+ | 3+ | CHI | ± | + | 2+ | 3+ | 4+ | CHI |
| 0ppm | 39 | 36 | 1 | 0 | 0 | 2 | | 39 | 0 | 0 | 0 | 0 | |
| 3ppm | 38 | 37 | 0 | 0 | 0 | 1 | | 38 | 0 | 0 | 0 | 0 | |
| 6ppm | 40 | 37 | 1 | 1 | 1 | 0 | | 40 | 0 | 0 | 0 | 0 | |
| 12ppm | 40 | 38 | 1 | 0 | 0 | 1 | | 40 | 0 | 0 | 0 | 0 | |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3

APPENDIX G 1

GROSS FINDINGS: SUMMARY, RAT: MALE: ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|-------------|------------------------------|------|-------|------|-------|------|------|-------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| skin/app | brown zone | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | nodule | | 6 | (12) | 2 | (4) | 3 | (6) | 3 | (6) |
| | mass | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | scab | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| subcutis | mass | | 9 | (18) | 9 | (18) | 3 | (6) | 7 | (14) |
| lung | white patch | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | white zone | | 3 | (6) | 0 | (0) | 1 | (2) | 1 | (2) |
| | red zone | | 0 | (0) | 2 | (4) | 0 | (0) | 0 | (0) |
| | red patch | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | nodule | | 2 | (4) | 0 | (0) | 1 | (2) | 2 | (4) |
| | adhesion | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| lymph node | enlarged | | 0 | (0) | 2 | (4) | 1 | (2) | 2 | (4) |
| spleen | enlarged | | 3 | (6) | 7 | (14) | 4 | (8) | 6 | (12) |
| | nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | deformed | | 1 | (2) | 2 | (4) | 1 | (2) | 0 | (0) |
| heart | white | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| tongue | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| esophagus | dilated | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| forestomach | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 1 | (2) |
| | ulcer | | 1 | (2) | 0 | (0) | 1 | (2) | 1 | (2) |
| gl stomach | ulcer | | 1 | (2) | 0 | (0) | 1 | (2) | 0 | (0) |
| | erosion | | 1 | (2) | 1 | (2) | 1 | (2) | 0 | (0) |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 2

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|------------------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| stomach | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| small intes | nodule | | 1 | (2) | 2 | (4) | 0 | (0) | 0 | (0) |
| | dilated | | 1 | (2) | 1 | (2) | 0 | (0) | 0 | (0) |
| | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| large intes | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| liver | enlarged | | 0 | (0) | 1 | (2) | 2 | (4) | 1 | (2) |
| | pale | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | nodule | | 0 | (0) | 2 | (4) | 0 | (0) | 2 | (4) |
| | rough | | 0 | (0) | 2 | (4) | 0 | (0) | 0 | (0) |
| | herniation | | 4 | (8) | 8 | (16) | 4 | (8) | 4 | (8) |
| pancreas | nodule | | 1 | (2) | 0 | (0) | 2 | (4) | 1 | (2) |
| kidney | cyst | | 0 | (0) | 1 | (2) | 0 | (0) | 1 | (2) |
| | granular | | 7 | (14) | 11 | (22) | 8 | (16) | 3 | (6) |
| urin bladd | urine:marked retention | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | fluid:transparent | | 0 | (0) | 1 | (2) | 1 | (2) | 0 | (0) |
| pituitary | enlarged | | 8 | (16) | 5 | (10) | 3 | (6) | 6 | (12) |
| | red zone | | 2 | (4) | 3 | (6) | 5 | (10) | 5 | (10) |
| | nodule | | 1 | (2) | 3 | (6) | 4 | (8) | 5 | (10) |
| | cyst | | 0 | (0) | 1 | (2) | 0 | (0) | 1 | (2) |
| thyroid | enlarged | | 6 | (12) | 7 | (14) | 4 | (8) | 3 | (6) |
| | nodule | | 1 | (2) | 2 | (4) | 5 | (10) | 3 | (6) |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|---------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| adrenal | enlarged | | 1 | (2) | 1 | (2) | 1 | (2) | 1 | (2) |
| testis | atrophic | | 5 | (10) | 6 | (12) | 0 | (0) | 2 | (4) |
| | nodule | | 41 | (82) | 40 | (80) | 40 | (80) | 34 | (68) |
| semin ves | enlarged | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| brain | hemorrhage | | 0 | (0) | 1 | (2) | 1 | (2) | 0 | (0) |
| eye | white | | 1 | (2) | 3 | (6) | 3 | (6) | 1 | (2) |
| | red | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| Zymbal gl | nodule | | 1 | (2) | 1 | (2) | 1 | (2) | 0 | (0) |
| pleura | nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| mediastinum | mass | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| peritoneum | nodule | | 0 | (0) | 3 | (6) | 1 | (2) | 0 | (0) |
| retroperit | cyst | | 1 | (2) | 1 | (2) | 0 | (0) | 1 | (2) |
| abdominal c | hemorrhage | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | ascites | | 0 | (0) | 4 | (8) | 0 | (0) | 0 | (0) |
| thoracic ca | mass | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | pleural fluid | | 0 | (0) | 2 | (4) | 1 | (2) | 0 | (0) |
| other | tail:nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| whole body | anemic | | 0 | (0) | 1 | (2) | 0 | (0) | 1 | (2) |

APPENDIX G2

GROSS FINDINGS: SUMMARY, RAT: MALE: DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|-------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 11 | (%) | 11 | (%) | 5 | (%) | 12 | (%) |
| skin/app | brown zone | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| | nodule | | 2 | (18) | 0 | (0) | 0 | (0) | 0 | (0) |
| | mass | | 0 | (0) | 0 | (0) | 1 | (20) | 0 | (0) |
| | scab | | 0 | (0) | 0 | (0) | 1 | (20) | 0 | (0) |
| subcutis | mass | | 1 | (9) | 3 | (27) | 1 | (20) | 2 | (17) |
| lung | white patch | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| | red zone | | 0 | (0) | 2 | (18) | 0 | (0) | 0 | (0) |
| | red patch | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| | nodule | | 2 | (18) | 0 | (0) | 0 | (0) | 0 | (0) |
| | adhesion | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| lymph node | enlarged | | 0 | (0) | 2 | (18) | 0 | (0) | 2 | (17) |
| spleen | enlarged | | 1 | (9) | 5 | (45) | 2 | (40) | 4 | (33) |
| | nodule | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| | deformed | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| heart | white | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| esophagus | dilated | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| forestomach | nodule | | 1 | (9) | 0 | (0) | 0 | (0) | 1 | (8) |
| | ulcer | | 1 | (9) | 0 | (0) | 0 | (0) | 1 | (8) |
| stomach | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| small intes | nodule | | 1 | (9) | 2 | (18) | 0 | (0) | 0 | (0) |
| | dilated | | 1 | (9) | 1 | (9) | 0 | (0) | 0 | (0) |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 2

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|------------------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 11 | (%) | 11 | (%) | 5 | (%) | 12 | (%) |
| small intes | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| large intes | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| liver | enlarged | | 0 | (0) | 1 | (9) | 2 | (40) | 1 | (8) |
| | pale | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| | nodule | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| | herniation | | 0 | (0) | 2 | (18) | 0 | (0) | 1 | (8) |
| kidney | cyst | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| | granular | | 3 | (27) | 1 | (9) | 0 | (0) | 1 | (8) |
| urin bladd | urine:marked retention | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| | fluid:transparent | | 0 | (0) | 1 | (9) | 1 | (20) | 0 | (0) |
| pituitary | enlarged | | 5 | (45) | 2 | (18) | 0 | (0) | 4 | (33) |
| | red zone | | 0 | (0) | 1 | (9) | 0 | (0) | 1 | (8) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| thyroid | enlarged | | 2 | (18) | 2 | (18) | 0 | (0) | 1 | (8) |
| | nodule | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| adrenal | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (8) |
| testis | atrophic | | 4 | (36) | 4 | (36) | 0 | (0) | 2 | (17) |
| | nodule | | 4 | (36) | 3 | (27) | 2 | (40) | 3 | (25) |
| semin ves | enlarged | | 0 | (0) | 0 | (0) | 1 | (20) | 0 | (0) |
| brain | hemorrhage | | 0 | (0) | 1 | (9) | 1 | (20) | 0 | (0) |
| eye | white | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 3

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|---------------|------------------------------|------|------|------|-------|------|-------|-------|------|
| | | | 11 | (%) | 11 | (%) | 5 | (%) | 12 | (%) |
| eye | red | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| Zymbal gl | nodule | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| mediastinum | mass | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| peritoneum | nodule | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| retroperit | cyst | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| abdominal c | hemorrhage | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |
| | ascites | | 0 | (0) | 2 | (18) | 0 | (0) | 0 | (0) |
| thoracic ca | mass | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| | pleural fluid | | 0 | (0) | 2 | (18) | 1 | (20) | 0 | (0) |
| whole body | anemic | | 0 | (0) | 1 | (9) | 0 | (0) | 0 | (0) |

(HPT080)

BAIS 3

APPENDIX G 3

GROSS FINDINGS: SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 39 | (%) | 39 | (%) | 45 | (%) | 38 | (%) |
| skin/app | nodule | | 4 | (10) | 2 | (5) | 3 | (7) | 3 | (8) |
| subcutis | mass | | 8 | (21) | 6 | (15) | 2 | (4) | 5 | (13) |
| lung | white zone | | 3 | (8) | 0 | (0) | 1 | (2) | 0 | (0) |
| | nodule | | 0 | (0) | 0 | (0) | 1 | (2) | 2 | (5) |
| lymph node | enlarged | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| spleen | enlarged | | 2 | (5) | 2 | (5) | 2 | (4) | 2 | (5) |
| | deformed | | 0 | (0) | 2 | (5) | 1 | (2) | 0 | (0) |
| tongue | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (3) |
| forestomach | ulcer | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| gl stomach | ulcer | | 1 | (3) | 0 | (0) | 1 | (2) | 0 | (0) |
| | erosion | | 1 | (3) | 1 | (3) | 1 | (2) | 0 | (0) |
| liver | nodule | | 0 | (0) | 1 | (3) | 0 | (0) | 2 | (5) |
| | rough | | 0 | (0) | 2 | (5) | 0 | (0) | 0 | (0) |
| | herniation | | 4 | (10) | 6 | (15) | 4 | (9) | 3 | (8) |
| pancreas | nodule | | 1 | (3) | 0 | (0) | 2 | (4) | 1 | (3) |
| kidney | cyst | | 0 | (0) | 1 | (3) | 0 | (0) | 0 | (0) |
| | granular | | 4 | (10) | 10 | (26) | 8 | (18) | 2 | (5) |
| pituitary | enlarged | | 3 | (8) | 3 | (8) | 3 | (7) | 2 | (5) |
| | red zone | | 2 | (5) | 2 | (5) | 5 | (11) | 4 | (11) |
| | nodule | | 1 | (3) | 3 | (8) | 4 | (9) | 4 | (11) |
| | cyst | | 0 | (0) | 1 | (3) | 0 | (0) | 1 | (3) |
| thyroid | enlarged | | 4 | (10) | 5 | (13) | 4 | (9) | 2 | (5) |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 2

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|-------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 39 | (%) | 39 | (%) | 45 | (%) | 38 | (%) |
| thyroid | nodule | | 0 | (0) | 2 | (5) | 5 | (11) | 3 | (8) |
| adrenal | enlarged | | 1 | (3) | 1 | (3) | 1 | (2) | 0 | (0) |
| testis | atrophic | | 1 | (3) | 2 | (5) | 0 | (0) | 0 | (0) |
| | nodule | | 37 | (95) | 37 | (95) | 38 | (84) | 31 | (82) |
| eye | white | | 1 | (3) | 2 | (5) | 3 | (7) | 1 | (3) |
| Zymbal gl | nodule | | 0 | (0) | 1 | (3) | 1 | (2) | 0 | (0) |
| pleura | nodule | | 0 | (0) | 1 | (3) | 0 | (0) | 0 | (0) |
| peritoneum | nodule | | 0 | (0) | 2 | (5) | 1 | (2) | 0 | (0) |
| retroperit | cyst | | 0 | (0) | 1 | (3) | 0 | (0) | 1 | (3) |
| abdominal c | ascites | | 0 | (0) | 2 | (5) | 0 | (0) | 0 | (0) |
| other | tail:nodule | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| whole body | anemic | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (3) |

(HPT080)

BAIS 3

APPENDIX G 4

GROSS FINDINGS: SUMMARY, RAT: FEMALE: ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|-------------|------------------------------|------|-------|------|-------|------|------|-------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| skin/app | colored | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | nodule | | 1 | (2) | 2 | (4) | 1 | (2) | 0 | (0) |
| subcutis | edema | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | mass | | 11 | (22) | 12 | (24) | 4 | (8) | 6 | (12) |
| lung | red | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | white zone | | 1 | (2) | 0 | (0) | 2 | (4) | 1 | (2) |
| | red zone | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | edema | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 1 | (2) |
| | voluminus | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | enlarged | | 0 | (0) | 1 | (2) | 2 | (4) | 0 | (0) |
| | enlarged | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| spleen | enlarged | | 5 | (10) | 8 | (16) | 3 | (6) | 3 | (6) |
| | white zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (4) |
| forestomach | ulcer | | 1 | (2) | 1 | (2) | 1 | (2) | 1 | (2) |
| gl stomach | ulcer | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | erosion | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| small intes | nodule | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| liver | white patch | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | yellow zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 5

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|------------|------------------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| liver | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | mass | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | rough | | 2 | (4) | 0 | (0) | 0 | (0) | 1 | (2) |
| | granular | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | herniation | | 7 | (14) | 9 | (18) | 11 | (22) | 8 | (16) |
| kidney | white patch | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (2) | 2 | (4) | 0 | (0) |
| | granular | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| urin bladd | urine:marked retention | | 1 | (2) | 0 | (0) | 2 | (4) | 0 | (0) |
| | urine:red | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| pituitary | enlarged | | 7 | (14) | 12 | (24) | 9 | (18) | 8 | (16) |
| | red zone | | 9 | (18) | 10 | (20) | 4 | (8) | 12 | (24) |
| | nodule | | 9 | (18) | 4 | (8) | 9 | (18) | 5 | (10) |
| | cyst | | 2 | (4) | 0 | (0) | 3 | (6) | 1 | (2) |
| thyroid | enlarged | | 2 | (4) | 2 | (4) | 0 | (0) | 0 | (0) |
| | nodule | | 0 | (0) | 2 | (4) | 0 | (0) | 2 | (4) |
| ovary | enlarged | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| uterus | nodule | | 3 | (6) | 8 | (16) | 5 | (10) | 6 | (12) |
| | mass | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | cyst | | 1 | (2) | 1 | (2) | 0 | (0) | 1 | (2) |
| | dilated lumen | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| vagina | fluid:black | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 6

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|------------------|------------------------------|------|------|------|-------|------|------|-------|------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| prep/cli gl | nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| brain | red zone | | 2 | (4) | 1 | (2) | 1 | (2) | 0 | (0) |
| | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| eye | white | | 2 | (4) | 8 | (16) | 4 | (8) | 2 | (4) |
| mediastinum | mass | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| abdominal c | ascites | | 2 | (4) | 0 | (0) | 1 | (2) | 1 | (2) |
| mesenterium | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| adipose | nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| thoracic ca | pleural fluid | | 0 | (0) | 0 | (0) | 2 | (4) | 0 | (0) |
| other | ear:nodule | | 0 | (0) | 0 | (0) | 1 | (2) | 1 | (2) |
| | lower jaw:nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| whole body | anemic | | 1 | (2) | 1 | (2) | 0 | (0) | 0 | (0) |

(HPT080)

BAIS 3

APPENDIX G 5

GROSS FINDINGS: SUMMARY, RAT: FEMALE: DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 4

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|-------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 11 | (%) | 12 | (%) | 10 | (%) | 10 | (%) |
| skin/app | colored | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) |
| | nodule | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |
| subcutis | edema | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) |
| | mass | | 2 | (18) | 4 | (33) | 0 | (0) | 2 | (20) |
| lung | red | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 0 | (0) | 2 | (20) | 1 | (10) |
| | red zone | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |
| | edema | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) |
| | voluminous | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) |
| lymph node | enlarged | | 0 | (0) | 1 | (8) | 2 | (20) | 0 | (0) |
| thymus | enlarged | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| spleen | enlarged | | 4 | (36) | 5 | (42) | 2 | (20) | 3 | (30) |
| | white zone | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (20) |
| forestomach | ulcer | | 1 | (9) | 1 | (8) | 1 | (10) | 1 | (10) |
| gl stomach | ulcer | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) |
| liver | yellow zone | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) |
| | rough | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| | granular | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) |
| | herniation | | 0 | (0) | 4 | (33) | 4 | (40) | 3 | (30) |
| kidney | white patch | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 5

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|------------------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 11 | (%) | 12 | (%) | 10 | (%) | 10 | (%) |
| kidney | white zone | | 0 | (0) | 1 | (8) | 2 | (20) | 0 | (0) |
| urin bladd | urine:marked retention | | 1 | (9) | 0 | (0) | 2 | (20) | 0 | (0) |
| pituitary | enlarged | | 3 | (27) | 4 | (33) | 4 | (40) | 3 | (30) |
| | red zone | | 0 | (0) | 1 | (8) | 0 | (0) | 1 | (10) |
| | nodule | | 1 | (9) | 1 | (8) | 2 | (20) | 0 | (0) |
| thyroid | nodule | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |
| ovary | enlarged | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |
| uterus | nodule | | 0 | (0) | 2 | (17) | 2 | (20) | 4 | (40) |
| | dilated lumen | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |
| prep/cli gl | nodule | | 0 | (0) | 1 | (8) | 0 | (0) | 0 | (0) |
| brain | red zone | | 2 | (18) | 1 | (8) | 0 | (0) | 0 | (0) |
| | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) |
| eye | white | | 0 | (0) | 0 | (0) | 1 | (10) | 1 | (10) |
| mediastinum | mass | | 1 | (9) | 0 | (0) | 0 | (0) | 0 | (0) |
| abdominal c | ascites | | 1 | (9) | 0 | (0) | 1 | (10) | 1 | (10) |
| thoracic ca | pleural fluid | | 0 | (0) | 0 | (0) | 2 | (20) | 0 | (0) |
| whole body | anemic | | 1 | (9) | 1 | (8) | 0 | (0) | 0 | (0) |

APPENDIX G 6

GROSS FINDINGS: SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 3

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|-------------|------------------------------|------|-------|------|-------|------|-------|-------|-------|
| | | | 39 | (%) | 38 | (%) | 40 | (%) | 40 | (%) |
| skin/app | nodule | | 1 | (3) | 1 | (3) | 1 | (3) | 0 | (0) |
| subcutis | mass | | 9 | (23) | 8 | (21) | 4 | (10) | 4 | (10) |
| lung | white zone | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| | nodule | | 1 | (3) | 0 | (0) | 0 | (0) | 1 | (3) |
| spleen | enlarged | | 1 | (3) | 3 | (8) | 1 | (3) | 0 | (0) |
| gl stomach | erosion | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| small intes | nodule | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| liver | white patch | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (3) | 0 | (0) | 0 | (0) |
| | mass | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| | rough | | 1 | (3) | 0 | (0) | 0 | (0) | 1 | (3) |
| | herniation | | 7 | (18) | 5 | (13) | 7 | (18) | 5 | (13) |
| kidney | granular | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| urin bladd | urine:red | | 0 | (0) | 1 | (3) | 0 | (0) | 0 | (0) |
| pituitary | enlarged | | 4 | (10) | 8 | (21) | 5 | (13) | 5 | (13) |
| | red zone | | 9 | (23) | 9 | (24) | 4 | (10) | 11 | (28) |
| | nodule | | 8 | (21) | 3 | (8) | 7 | (18) | 5 | (13) |
| | cyst | | 2 | (5) | 0 | (0) | 3 | (8) | 1 | (3) |
| thyroid | enlarged | | 2 | (5) | 2 | (5) | 0 | (0) | 0 | (0) |
| | nodule | | 0 | (0) | 1 | (3) | 0 | (0) | 2 | (5) |
| uterus | nodule | | 3 | (8) | 6 | (16) | 3 | (8) | 2 | (5) |
| | mass | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 4

| Organ | Findings | Group Name NO. of Animals | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|-------------|------------------|------------------------------|------|------|------|-------|------|------|-------|------|
| | | | 39 | (%) | 38 | (%) | 40 | (%) | 40 | (%) |
| uterus | cyst | | 1 | (3) | 1 | (3) | 0 | (0) | 1 | (3) |
| vagina | fluid:black | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| brain | red zone | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| eye | white | | 2 | (5) | 8 | (21) | 3 | (8) | 1 | (3) |
| abdominal c | ascites | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| mesenterium | nodule | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| adipose | nodule | | 0 | (0) | 1 | (3) | 0 | (0) | 0 | (0) |
| other | ear:nodule | | 0 | (0) | 0 | (0) | 1 | (3) | 1 | (3) |
| | lower jaw:nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (3) |

(HPT080)

BAIS 3

APPENDIX H 1

ORGAN WEIGHT , ABSOLUTE: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (105W)

PAGE : 1

| Group Name | NO. of Animals | Body Weight | | ADRENALS | | TESTES | | HEART | | LUNGS | | KIDNEYS | |
|------------|-------------------|-------------|------|----------|-------|--------|-------|--------|-------|--------|-------|---------|--------|
| 0ppm | 39 | 381± | 55 | 0.076± | 0.023 | 3.776± | 1.510 | 1.279± | 0.155 | 1.434± | 0.271 | 2.806± | 0.289 |
| 3ppm | 39 | 376± | 37 | 0.111± | 0.231 | 3.552± | 1.233 | 1.270± | 0.107 | 1.534± | 0.497 | 2.896± | 0.463 |
| 6ppm | 45 | 362± | 31 | 0.076± | 0.036 | 3.181± | 1.498 | 1.234± | 0.119 | 1.410± | 0.146 | 2.787± | 0.309 |
| 12ppm | 38 | 345± | 32** | 0.072± | 0.013 | 3.416± | 1.631 | 1.234± | 0.102 | 1.427± | 0.185 | 2.652± | 0.203* |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (105W)

PAGE : 2

| Group Name | NO. of Animals | SPLEEN | | LIVER | | BRAIN | |
|------------|-------------------|--------|-------|---------|---------|--------|-------|
| 0ppm | 39 | 1.141± | 0.946 | 11.248± | 1.610 | 2.009± | 0.061 |
| 3ppm | 39 | 1.369± | 1.949 | 11.691± | 2.477 | 2.008± | 0.076 |
| 6ppm | 45 | 1.152± | 1.283 | 10.725± | 1.878 | 2.003± | 0.054 |
| 12ppm | 38 | 1.067± | 0.833 | 10.438± | 2.665** | 1.992± | 0.062 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

APPENDIX H2

ORGAN WEIGHT , ABSOLUTE: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of Animals | Body Weight | ADRENALS | OVARIES | HEART | LUNGS | KIDNEYS |
|------------|-------------------|-------------|--------------|--------------|--------------|--------------|----------------|
| 0ppm | 39 | 255± 23 | 0.076± 0.021 | 0.123± 0.025 | 0.876± 0.069 | 1.004± 0.082 | 1.813± 0.183 |
| 3ppm | 38 | 253± 19 | 0.072± 0.013 | 0.118± 0.018 | 0.885± 0.087 | 1.019± 0.117 | 1.770± 0.154 |
| 6ppm | 40 | 250± 21 | 0.072± 0.009 | 0.114± 0.022 | 0.869± 0.058 | 0.988± 0.083 | 1.746± 0.110 |
| 12ppm | 40 | 230± 20** | 0.072± 0.009 | 0.125± 0.067 | 0.877± 0.061 | 0.977± 0.053 | 1.700± 0.116** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (105W)

PAGE : 4

| Group Name | NO. of Animals | SPLEEN | | LIVER | | BRAIN | |
|------------|-------------------|--------|--------|--------|---------|--------|--------|
| 0ppm | 39 | 0.560± | 0.266 | 6.539± | 0.872 | 1.820± | 0.042 |
| 3ppm | 38 | 1.086± | 2.580 | 6.657± | 1.429 | 1.830± | 0.058 |
| 6ppm | 40 | 0.651± | 0.794 | 6.231± | 0.656 | 1.846± | 0.061* |
| 12ppm | 40 | 0.467± | 0.132* | 5.947± | 0.723** | 1.835± | 0.042 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

APPENDIX I 1

ORGAN WEIGHT, RELATIVE: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (105W)

PAGE : 1

| Group Name | NO. of Animals | Body Weight (g) | ADRENALS | TESTES | HEART | LUNGS | KIDNEYS |
|------------|-------------------|--------------------|--------------|--------------|--------------|----------------|--------------|
| 0ppm | 39 | 381± 55 | 0.020± 0.007 | 1.003± 0.408 | 0.338± 0.032 | 0.382± 0.090 | 0.746± 0.104 |
| 3ppm | 39 | 376± 37 | 0.030± 0.067 | 0.946± 0.321 | 0.340± 0.037 | 0.412± 0.148 | 0.779± 0.176 |
| 6ppm | 45 | 362± 31 | 0.021± 0.010 | 0.877± 0.417 | 0.344± 0.045 | 0.393± 0.057 | 0.775± 0.102 |
| 12ppm | 38 | 345± 32** | 0.021± 0.004 | 0.988± 0.471 | 0.360± 0.038 | 0.417± 0.074** | 0.772± 0.070 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (105W)

PAGE : 2

| Group Name | NO. of Animals | SPLEEN | LIVER | BRAIN |
|------------|-------------------|--------------|--------------|----------------|
| 0ppm | 39 | 0.306± 0.279 | 2.970± 0.350 | 0.535± 0.052 |
| 3ppm | 39 | 0.373± 0.559 | 3.128± 0.725 | 0.538± 0.046 |
| 6ppm | 45 | 0.327± 0.398 | 2.979± 0.594 | 0.557± 0.049 |
| 12ppm | 38 | 0.314± 0.267 | 3.040± 0.831 | 0.581± 0.053** |

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

APPENDIX 12

ORGAN WEIGHT, RELATIVE: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of Animals | Body Weight (g) | ADRENALS | OVARIES | HEART | LUNGS | KIDNEYS |
|------------|-------------------|--------------------|--------------|--------------|----------------|---------------|--------------|
| 0ppm | 39 | 255± 23 | 0.030± 0.007 | 0.048± 0.009 | 0.345± 0.025 | 0.397± 0.049 | 0.717± 0.102 |
| 3ppm | 38 | 253± 19 | 0.029± 0.006 | 0.047± 0.007 | 0.351± 0.038 | 0.404± 0.055 | 0.701± 0.073 |
| 6ppm | 40 | 250± 21 | 0.029± 0.004 | 0.046± 0.010 | 0.350± 0.034 | 0.398± 0.041 | 0.703± 0.081 |
| 12ppm | 40 | 230± 20** | 0.031± 0.005 | 0.054± 0.027 | 0.382± 0.031** | 0.427± 0.048* | 0.742± 0.071 |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (105W)

PAGE : 4

| Group Name | NO. of Animals | SPLEEN | LIVER | BRAIN |
|------------|-------------------|--------------|--------------|----------------|
| 0ppm | 39 | 0.222± 0.110 | 2.575± 0.353 | 0.720± 0.063 |
| 3ppm | 38 | 0.435± 1.038 | 2.634± 0.573 | 0.725± 0.045 |
| 6ppm | 40 | 0.259± 0.290 | 2.507± 0.296 | 0.745± 0.068 |
| 12ppm | 40 | 0.203± 0.058 | 2.588± 0.294 | 0.803± 0.081** |

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

APPENDIX J 1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY,
RAT: MALE: ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|----------------|--|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | 50 | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | | | | |
| skin/app | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | abscess | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | scab | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) |
| | epidermal cyst | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| subcutis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cyst | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | abscess | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | edema | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 2

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|--|---------------------------------------|--------|--------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|-------|-------|-------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | | | | | | | | | | | | | | | | | | | |
| | thrombus | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | squamous cell hyperplasia | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | 0 | * |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (4) | (2) | (0) | (0) | (12) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:gland | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | goblet cell hyperplasia | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | 16 | 13 | 9 | 0 | 12 | 24 | 4 | 0 | 26 | 9 | 4 | 0 | 12 | 13 | 3 | 0 | 0 | 0 | 0 | 0 |
| | | (32) | (26) | (18) | (0) | (24) | (48) | (8) | (0) | (52) | (18) | (8) | (0) | (24) | (26) | (6) | (0) | (0) | (0) | (0) | (0) |
| | eosinophilic change:respiratory epithelium | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (8) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation:foreign body | 19 | 5 | 0 | 0 | 16 | 4 | 2 | 0 | 11 | 1 | 4 | 0 | 20 | 15 | 7 | 0 | 0 | 0 | 0 | ** |
| | | (38) | (10) | (0) | (0) | (32) | (8) | (4) | (0) | (22) | (2) | (8) | (0) | (40) | (30) | (14) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|---|---------------------------------------|-----------|-----------|-----------|-------------|-----------|-----------|--------------|-------------|-------------|-----------|--------------|-------------|-------------|-------------|--------------|-------|-----|-----|-----|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation:respiratory epithelium | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 7 (14) | 1 (2) | 0 (0) | 0 * (0) | 24 (48) | 1 (2) | 0 (0) | 0 ** (0) | 19 (38) | 23 (46) | 0 (0) | 0 ** (0) | | | | |
| | respiratory metaplasia:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 8 (16) | 0 (0) | 0 (0) | 0 ** (0) | 5 (10) | 3 (6) | 0 (0) | 0 * (0) | 5 (10) | 2 (4) | 1 (2) | 0 * (0) | | | | |
| | squamous cell metaplasia:respiratory epithelium | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 11 (22) | 3 (6) | 1 (2) | 0 ** (0) | 29 (58) | 17 (34) | 2 (4) | 0 ** (0) | 8 (16) | 21 (42) | 19 (38) | 0 ** (0) | | | | |
| | atrophy:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 6 (12) | 0 (0) | 0 * (0) | | | | |
| | necrosis:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 1 (2) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) | 0 (0) | | | | |
| | hyperplasia:respiratory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 1 (2) | 0 (0) | 24 (48) | 6 (12) | 2 (4) | 0 ** (0) | 10 (20) | 24 (48) | 6 (12) | 0 ** (0) | | | | |
| nasopharynx | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation:foreign body | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | | | | |
| larynx | | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | ulcer | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|-----------------------------|---------------------------------------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| larynx | inflammation | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 6 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (12) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| trachea | inflammation | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| lung | congestion | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | edema | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | thrombus | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | osseous metaplasia | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (4) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | accumulation of foamy cells | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 5

| | | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|---------------------------------------|---------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|-------|-------|-------|-------|--|--|--|
| | | 50 | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | | | |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | | | |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| lung | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | | | |
| | bronchiolar-alveolar cell hyperplasia | | 4 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | | | |
| | | | (8) | (4) | (0) | (0) | (2) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (2) | (0) | (0) | | | |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | | | |
| | granulation | | 2 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 5 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | | | |
| | | | (4) | (0) | (0) | (0) | (8) | (2) | (0) | (0) | (10) | (4) | (0) | (0) | (0) | (6) | (0) | (0) | | | |
| | increased hematopoiesis | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | | | |
| | decreased hematopoiesis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | | | |
| lymph node | | | <50> | | | | <49> | | | | <50> | | | | <50> | | | | | | |
| | cyst | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| | | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | |
| | lymphadenitis | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 6

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|------------------------------|---------------------------------------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | | | | |
| spleen | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) |
| | deposit of hemosiderin | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | fibrosis | 1 | 1 | 0 | 0 | 3 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (2) | (0) | (0) | (6) | (0) | (2) | (0) | (2) | (2) | (0) | (0) | (2) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | 6 | 2 | 0 | 0 | 5 | 4 | 1 | 0 | 6 | 2 | 2 | 0 | 6 | 2 | 2 | 0 | 5 | 1 | 1 | 0 |
| | | (12) | (4) | (0) | (0) | (10) | (8) | (2) | (0) | (12) | (4) | (4) | (0) | (12) | (4) | (4) | (0) | (10) | (2) | (2) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | | | | |
| heart | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | myocardial fibrosis | 31 | 1 | 0 | 0 | 27 | 1 | 0 | 0 | 26 | 0 | 0 | 0 | 31 | 0 | 0 | 0 | 31 | 1 | 0 | 0 |
| | | (62) | (2) | (0) | (0) | (54) | (2) | (0) | (0) | (52) | (0) | (0) | (0) | (62) | (0) | (0) | (0) | (62) | (2) | (0) | (0) |
| artery/aort | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | arteritis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|---------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| tooth | inflammation | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| tongue | ulcer | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | arteritis | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| esophagus | dilatation | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| stomach | mineralization | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammatory infiltration | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | basal cell activation | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 8

| Organ | Findings | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|------|------|------|------|-------|------|------|------|------|------|------|------|-------|------|------|------|
| | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | |
| stomach | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | erosion:forestomach | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | ulcer:forestomach | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (2) | (0) | (0) |
| | hyperplasia:forestomach | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (2) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | erosion:glandular stomach | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | ulcer:glandular stomach | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| small intes | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | ulcer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| liver | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | herniation | 4 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 9

| | | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-----------------------|---------------------------------------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--|--|--|
| | | 50 | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | | | |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | | | |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| liver | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | | | |
| | necrosis:central | | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | | | |
| | fatty change:central | | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | | | |
| | | | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | | | |
| | granulation | | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | | | |
| | | | (8) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | | | |
| | clear cell focus | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | |
| | basophilic cell focus | | 10 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | | | |
| | | | (20) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | | | |
| | spongiosis hepatitis | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | |
| | bile duct hyperplasia | | 43 | 2 | 0 | 0 | 44 | 1 | 0 | 0 | 43 | 1 | 0 | 0 | 41 | 2 | 0 | 0 | | | |
| | | | (86) | (4) | (0) | (0) | (88) | (2) | (0) | (0) | (86) | (2) | (0) | (0) | (82) | (4) | (0) | (0) | | | |
| pancreas | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | | | |
| | atrophy | | 9 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 9 | 1 | 0 | 0 | 4 | 1 | 0 | 0 | | | |
| | | | (18) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (18) | (2) | (0) | (0) | (8) | (2) | (0) | (0) | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 10

| Organ | Findings | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-------------------------------|-------------------------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|
| | | Group Name | | | | 50 | | | | 50 | | | | 50 | | | |
| | | No. of Animals on Study | | | | Grade | | | | Grade | | | | Grade | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | |
| pancreas | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | islet cell hyperplasia | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | hyperplasia:acinar cell | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | |
| kidney | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cyst | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | hyaline droplet | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | chronic nephropathy | 7 | 27 | 12 | 0 | 8 | 19 | 18 | 2 | 6 | 21 | 19 | 2 | 18 | 17 | 8 | 1 |
| | | (14) | (54) | (24) | (0) | (16) | (38) | (36) | (4) | (12) | (42) | (38) | (4) | (36) | (34) | (16) | (2) |
| | mineralization:pelvis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | urothelial hyperplasia:pelvis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) -
 ALL ANIMALS (0-105W)

PAGE : 11

| Organ | Findings | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|--|-------------------------|------|------|------|---------|------|------|------|---------|------|------|------|---------|------|------|------|
| | | No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | | | | 1 2 3 4 | | | | 1 2 3 4 | | | | 1 2 3 4 | | | |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | |
| urin bladd | simple hyperplasia:transitional epithelium | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Endocrine system} | | | | | | | | | | | | | | | | | |
| pituitary | cyst | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | hyperplasia | 14 | 1 | 0 | 0 | 12 | 1 | 0 | 0 | 6 | 3 | 0 | 0 | 9 | 3 | 0 | 0 |
| | | (29) | (2) | (0) | (0) | (24) | (2) | (0) | (0) | (12) | (6) | (0) | (0) | (18) | (6) | (0) | (0) |
| | Rathke pouch | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| thyroid | C-cell hyperplasia | <50> | | | | <49> | | | | <50> | | | | <50> | | | |
| | | 8 | 4 | 0 | 0 | 8 | 0 | 0 | 0 | 5 | 3 | 0 | 0 | 7 | 3 | 0 | 0 |
| | | (16) | (8) | (0) | (0) | (16) | (0) | (0) | (0) | (10) | (6) | (0) | (0) | (14) | (6) | (0) | (0) |
| | focal follicular cell hyperplasia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 12

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|---------------------------|---------------------------------------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| parathyroid | | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cyst | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| adrenal | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia:cortical cell | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (2) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | hyperplasia:medulla | 7 | 1 | 0 | 0 | 3 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 * |
| | | (14) | (2) | (0) | (0) | (6) | (2) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (0) | (0) | (0) |
| | focal fatty change:cortex | 3 | 0 | 0 | 0 | 4 | 2 | 0 | 0 | 6 | 1 | 0 | 0 | 5 | 1 | 0 | 0 | 5 | 1 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (8) | (4) | (0) | (0) | (12) | (2) | (0) | (0) | (10) | (2) | (0) | (0) | (10) | (2) | (0) | (0) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| testis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | atrophy | 11 | 1 | 0 | 0 | 5 | 0 | 0 | 0 | 12 | 0 | 0 | 0 | 7 | 2 | 0 | 0 | 7 | 2 | 0 | 0 |
| | | (22) | (2) | (0) | (0) | (10) | (0) | (0) | (0) | (24) | (0) | (0) | (0) | (14) | (4) | (0) | (0) | (14) | (4) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 13

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|-------------------------------|---------------------------------------|-------|------|------|-------|------|------|------|-------|-------|------|------|-------|------|------|------|-------|------|------|------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| testis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | mineralization | 7 | 0 | 0 | 0 | 6 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 7 | 0 | 0 | 0 |
| | | (14) | (0) | (0) | (0) | (12) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (14) | (0) | (0) | (0) |
| | arteritis | 5 | 0 | 0 | 0 | 5 | 2 | 0 | 0 | 11 | 2 | 0 | 0 | 4 | 2 | 0 | 0 | 4 | 2 | 0 | 0 |
| | | (10) | (0) | (0) | (0) | (10) | (4) | (0) | (0) | (22) | (4) | (0) | (0) | (8) | (4) | (0) | (0) | (8) | (4) | (0) | (0) |
| | interstitial cell hyperplasia | 9 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 8 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | (16) | (0) | (0) | (0) |
| semin ves | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| prostate | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 15 | 4 | 0 | 0 | 10 | 1 | 0 | 0 | 15 | 2 | 1 | 0 | 18 | 0 | 0 | 0 | 18 | 0 | 0 | 0 |
| | | (30) | (8) | (0) | (0) | (20) | (2) | (0) | (0) | (30) | (4) | (2) | (0) | (36) | (0) | (0) | (0) | (36) | (0) | (0) | (0) |
| | hyperplasia | 9 | 7 | 0 | 0 | 7 | 3 | 0 | 0 | 9 | 5 | 0 | 0 | 8 | 4 | 0 | 0 | 8 | 4 | 0 | 0 |
| | | (18) | (14) | (0) | (0) | (14) | (6) | (0) | (0) | (18) | (10) | (0) | (0) | (16) | (8) | (0) | (0) | (16) | (8) | (0) | (0) |
| mammary gl | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | galactoceles | 4 | 0 | 0 | 0 | 6 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 7 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (12) | (0) | (2) | (0) | (2) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (14) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) -
 ALL ANIMALS (0-105W)

PAGE : 14

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--------------------------|---------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Nervous system} | | | | | | | | | | | | | | | | | | | | | |
| brain | necrosis:focal | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spinal cord | radiculoneuropathy | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | | | | |
| eye | cataract | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | retinal atrophy | 1 | 0 | 0 | 0 | 1 | 2 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (2) | (4) | (2) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) |
| Harder gl | degeneration | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | lymphocytic infiltration | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |

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 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
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STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 15

| | | Group Name | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|----------------|-------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| Harder gl | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | |
| muscle | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | mineralization | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | arteritis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| bone | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | fracture | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | osteosclerosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Body cavities} | | | | | | | | | | | | | | | | | | |
| pleura | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
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HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 16

| Organ | Findings | Group Name | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-------|----------|-------------------------|--|--|--|------|-----|-----|-----|------|-----|-----|-----|------|-----|-----|-----|-------|-----|-----|-----|
| | | No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

{Body cavities}

| | | | | | | | | | | | | | | | | | |
|-------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| mesenterium | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| arteritis | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

(HPT150)

BAIS3

APPENDIX J 2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY,
RAT: MALE: DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--|---------------------------------------|-------------|------------|------------|-------------|-------------|------------|------------|-------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | Grade | | | | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | | | | |
| skin/app | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | abscess | 1 (9) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | epidermal cyst | 1 (9) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | thrombus | 2 (18) | 0 (0) | 0 (0) | 0 (0) | 5 (45) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| | mineralization | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (9) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | squamous cell hyperplasia | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 1 (20) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| | eosinophilic change:olfactory epithelium | 2 (18) | 2 (18) | 1 (9) | 0 (0) | 2 (18) | 4 (36) | 0 (0) | 0 (0) | 3 (60) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 1 (8) | 1 (8) | 0 (0) | 1 (8) | 1 (8) | 1 (8) | 0 (0) |
| | eosinophilic change:respiratory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (9) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 2

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|---|--|-----------|-----------|-----------|------------|-----------|-----------|-----------|------------|------------|------------|-----------|------------|------------|------------|-----------|-------|-----|-----|-----|
| | | 11 | | | | 11 | | | | 5 | | | | 12 | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | inflammation:foreign body | 5 (45) | 1 (9) | 0 (0) | 0 (0) | 4 (36) | 1 (9) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 1 (20) | 0 (0) | 6 (50) | 1 (8) | 1 (8) | 0 (0) | | | | |
| | inflammation:respiratory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (40) | 0 (0) | 0 (0) | 0 (0) | 3 (25) | 4 (33) | 0 (0) | 0 (0) | ** | | | |
| | respiratory metaplasia:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (9) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 2 (17) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | squamous cell metaplasia:respiratory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (9) | 0 (0) | 0 (0) | 0 (0) | 3 (60) | 1 (20) | 1 (20) | 0 (0) | 2 (17) | 4 (33) | 5 (42) | 0 (0) | ** | | | |
| | atrophy:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 5 (42) | 0 (0) | 0 (0) | | | | |
| | necrosis:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 1 (20) | 0 (0) | 0 (0) | 1 (8) | 1 (8) | 0 (0) | 0 (0) | | | | |
| | hyperplasia:respiratory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 2 (40) | 2 (40) | 0 (0) | 2 (17) | 6 (50) | 2 (17) | 0 (0) | ** | | | |
| nasopharynx | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | inflammation:foreign body | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 3

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|-----------------------------|---------------------------------------|------|------|------|-------|------|------|------|------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | Grade | | | | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| larynx | ulcer | <11> | | | | <10> | | | | < 5> | | | | <12> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation | <11> | | | | <10> | | | | < 5> | | | | <12> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| trachea | inflammation | <11> | | | | <10> | | | | < 5> | | | | <12> | | | | | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| lung | congestion | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (42) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | edema | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | osseous metaplasia | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | accumulation of foamy cells | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 4

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|------------------------------|--|-------|-------|-------|--------|--------|-------|-------|-------|--------|--------|-------|--------|-------|-------|-------|-------|-------|-------|-------|
| | | 11 | | | | 11 | | | | 5 | | | | 12 | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | | | | |
| bone marrow | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | granulation | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | increased hematopoiesis | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (40) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | decreased hematopoiesis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| lymph node | | <11> | | | | <10> | | | | < 5> | | | | <12> | | | | | | | |
| | cyst | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spleen | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | deposit of hemosiderin | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (33) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | fibrosis | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | 2 | 1 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 1 | 2 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (18) | (9) | (0) | (0) | (0) | (27) | (9) | (0) | (0) | (20) | (40) | (0) | (8) | (0) | (8) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 5

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|---------------------------|--|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | thrombus | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | myocardial fibrosis | | | | | | | | | | | | | | | | | |
| | | | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (36) | (0) | (0) | (0) | (45) | (0) | (0) | (0) | (60) | (0) | (0) | (0) | (17) | (8) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| esophagus | dilatation | | <11> | | | | <10> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| stomach | mineralization | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammatory infiltration | | | | | | | | | | | | | | | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) |
| | erosion:forestomach | | | | | | | | | | | | | | | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 6

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|---------------------------------------|------------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|
| | | Grade | | | | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| stomach | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | ulcer:forestomach | 3 (27) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 1 (8) | 0 (0) | 0 (0) |
| | hyperplasia:forestomach | 0 (0) | 2 (18) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (17) | 0 (0) | 0 (0) | 0 (0) |
| | erosion:glandular stomach | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (18) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| | ulcer:glandular stomach | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| small intes | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | inflammation | 0 (0) | 1 (9) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| liver | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | herniation | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (18) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| | necrosis:central | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (27) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 1 (8) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 7

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-----------------------|---------------------------------------|-------|------|------|-------|------|------|------|-------|-------|------|------|-------|------|------|------|-------|------|------|------|
| | | Grade | | | | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| liver | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | fatty change:central | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (18) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) |
| | granulation | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | basophilic cell focus | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | spongiosis hepatitis | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | bile duct hyperplasia | 7 | 1 | 0 | 0 | 7 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 7 | 1 | 0 | 0 | 7 | 1 | 0 | 0 |
| | | (64) | (9) | (0) | (0) | (64) | (9) | (0) | (0) | (20) | (20) | (0) | (0) | (58) | (8) | (0) | (0) | (58) | (8) | (0) | (0) |
| pancreas | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | atrophy | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 * | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (60) | (20) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | | | | |
| kidney | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | cyst | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 8

| | | Group Name | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-----------------------|-------------------------|-------|--------|--------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | hyaline droplet | | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (9) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | chronic nephropathy | | 0 | 3 | 4 | 0 | 5 | 2 | 0 | 1 * | 3 | 1 | 0 | 0 * | 5 | 1 | 1 | 1 |
| | | | (0) | (27) | (36) | (0) | (45) | (18) | (0) | (9) | (60) | (20) | (0) | (0) | (42) | (8) | (8) | (8) |
| | mineralization:pelvis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | | | <10> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | hyperplasia | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | Rathke pouch | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | |
| thyroid | | | <11> | | | | <10> | | | | < 5> | | | | <12> | | | |
| | C-cell hyperplasia | | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (9) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (8) | (8) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 9

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|-------------------------------|--|-------|------|------|-------|------|------|------|-------|------|-------|------|-------|------|------|------|-------|------|------|------|
| | | 11 | | | | 11 | | | | 5 | | | | 12 | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| adrenal | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | hyperplasia:medulla | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (9) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | focal fatty change:cortex | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| testis | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | atrophy | 5 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (45) | (9) | (0) | (0) | (18) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (25) | (0) | (0) | (0) |
| | mineralization | 5 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (45) | (0) | (0) | (0) | (18) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (25) | (0) | (0) | (0) |
| | arteritis | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (27) | (0) | (0) | (0) | (27) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | interstitial cell hyperplasia | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (45) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (17) | (0) | (0) | (0) |
| prostate | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | | | | | |
| | inflammation | 2 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (18) | (27) | (0) | (0) | (9) | (0) | (0) | (0) | (20) | (0) | (20) | (0) | (25) | (0) | (0) | (0) | (25) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 10

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--------------------|--|-------|------|------|------|------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| prostate | hyperplasia | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) |
| mammary gl | galactoceles | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (27) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (33) | (0) | (0) | (0) |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | necrosis:focal | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spinal cord | radiculoneuropathy | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | cataract | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) : ...
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 11

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|-----------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | | 11 | | | | 11 | | | | 5 | | | | 12 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | retinal atrophy | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | |
| muscle | mineralization | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| bone | fracture | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Body cavities} | | | | | | | | | | | | | | | | | | |
| pleura | inflammation | | <11> | | | | <11> | | | | < 5> | | | | <12> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

(HPT150)

BAIS3

APPENDIX J 3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY,
RAT: MALE: SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|---------------------------|---------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|-------|-------|-------|-------|
| | | Grade | | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | | | | |
| skin/app | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | scab | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| subcutis | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | cyst | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | abscess | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | edema | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | squamous cell hyperplasia | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 13 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (2) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 2

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|---|---------------------------------------|--------|--------|-------|--------|--------|--------|-------|--------|--------|-------|-------|--------|--------|--------|-------|-------|-------|-------|-------|
| | | Grade | | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | hyperplasia:gland | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | | | | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | | | | |
| | goblet cell hyperplasia | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | 14 | 11 | 8 | 0 | 10 | 20 | 4 | 0 | 23 | 9 | 4 | 0 | 11 | 12 | 2 | 0 | | | | |
| | | (36) | (28) | (21) | (0) | (26) | (51) | (10) | (0) | (51) | (20) | (9) | (0) | (29) | (32) | (5) | (0) | | | | |
| | eosinophilic change:respiratory epithelium | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | | | | |
| | | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (8) | (3) | (0) | (0) | | | | |
| | inflammation:foreign body | 14 | 4 | 0 | 0 | 12 | 3 | 2 | 0 | 10 | 1 | 3 | 0 | 14 | 14 | 6 | 0 ** | | | | |
| | | (36) | (10) | (0) | (0) | (31) | (8) | (5) | (0) | (22) | (2) | (7) | (0) | (37) | (37) | (16) | (0) | | | | |
| | inflammation:respiratory epithelium | 1 | 0 | 0 | 0 | 7 | 1 | 0 | 0 * | 22 | 1 | 0 | 0 ** | 16 | 19 | 0 | 0 ** | | | | |
| | | (3) | (0) | (0) | (0) | (18) | (3) | (0) | (0) | (49) | (2) | (0) | (0) | (42) | (50) | (0) | (0) | | | | |
| | respiratory metaplasia:olfactory epithelium | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0 * | 4 | 3 | 0 | 0 * | 3 | 2 | 1 | 0 | | | | |
| | | (0) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (9) | (7) | (0) | (0) | (8) | (5) | (3) | (0) | | | | |
| | squamous cell metaplasia:respiratory epithelium | 1 | 0 | 0 | 0 | 10 | 3 | 1 | 0 ** | 26 | 16 | 1 | 0 ** | 6 | 17 | 14 | 0 ** | | | | |
| | | (3) | (0) | (0) | (0) | (26) | (8) | (3) | (0) | (58) | (36) | (2) | (0) | (16) | (45) | (37) | (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 3

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|------------------------------------|--|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|--------|-------|
| | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | atrophy:olfactory epithelium | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (3) | (3) | (0) | (0) |
| | necrosis:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 0 | 23 | 4 | 0 | 0 ** | 8 | 18 | 4 | 0 ** |
| | hyperplasia:respiratory epithelium | | (0) | (0) | (0) | (0) | (5) | (0) | (3) | (0) | (51) | (9) | (0) | (0) | (21) | (47) | (11) | (0) |
| nasopharynx | inflammation:foreign body | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| larynx | inflammation | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | | | 6 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (15) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| lung | thrombus | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | osseous metaplasia | | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (5) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 4

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|---------------------------------------|---------------------------------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | Grade | | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| lung | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | accumulation of foamy cells | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 (0) | 5 (11) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | bronchiolar-alveolar cell hyperplasia | 4 (10) | 2 (5) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | | | | |
| bone marrow | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | granulation | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 1 (3) | 0 (0) | 0 (0) | 5 (11) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | increased hematopoiesis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| lymph node | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | cyst | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | lymphadenitis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 5

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|------------------------------|--|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| spleen | | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | thrombus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) |
| | deposit of hemosiderin | | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | fibrosis | | 0 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (8) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | | 4 | 1 | 0 | 0 | 5 | 1 | 0 | 0 | 6 | 1 | 0 | 0 | 4 | 1 | 0 | 0 |
| | | | (10) | (3) | (0) | (0) | (13) | (3) | (0) | (0) | (13) | (2) | (0) | (0) | (11) | (3) | (0) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | myocardial fibrosis | | 27 | 1 | 0 | 0 | 22 | 1 | 0 | 0 | 23 | 0 | 0 | 0 | 29 | 0 | 0 | 0 |
| | | | (69) | (3) | (0) | (0) | (56) | (3) | (0) | (0) | (51) | (0) | (0) | (0) | (76) | (0) | (0) | (0) |
| artery/aort | | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | arteritis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 6

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-------------------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | 39 | | | | 39 | | | | 45 | | | | 38 | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| tooth | inflammation | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| tongue | ulcer | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | arteritis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| stomach | basal cell activation | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | erosion:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:forestomach | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 7

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|--|-----------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| | | 39 | | | | 39 | | | | 45 | | | | 38 | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| stomach | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | erosion:glandular stomach | 4 (10) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | ulcer:glandular stomach | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| small intes | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | ulcer | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| liver | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | herniation | 4 (10) | 0 (0) | 0 (0) | 0 (0) | 7 (18) | 0 (0) | 0 (0) | 0 (0) | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | granulation | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 (0) | 5 (11) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | clear cell focus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | basophilic cell focus | 10 (26) | 0 (0) | 0 (0) | 0 (0) | 6 (15) | 0 (0) | 0 (0) | 0 (0) | 4 (9) | 0 (0) | 0 (0) | 0 (0) | 4 (11) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 8

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-------------------------------|---------------------------------------|-------------|------------|-----------|-------------|-------------|-------------|-----------|-------------|-------------|-------------|-----------|-------------|-------------|------------|-----------|-------|--|--|--|
| | | Grade | | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | | | | |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | | | | |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| liver | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | bile duct hyperplasia | 36 (92) | 1 (3) | 0 (0) | 0 (0) | 37 (95) | 0 (0) | 0 (0) | 0 (0) | 42 (93) | 0 (0) | 0 (0) | 0 (0) | 34 (89) | 1 (3) | 0 (0) | 0 (0) | | | | |
| pancreas | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | atrophy | 7 (18) | 0 (0) | 0 (0) | 0 (0) | 7 (18) | 0 (0) | 0 (0) | 0 (0) | 6 (13) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 1 (3) | 0 (0) | 0 (0) | | | | |
| | islet cell hyperplasia | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | hyperplasia:acinar cell | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| {Urinary system} | | | | | | | | | | | | | | | | | | | | | |
| kidney | | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | chronic nephropathy | 7 (18) | 24 (62) | 8 (21) | 0 (0) | 3 (8) | 17 (44) | 18 (46) | 1 (3) | 3 (7) | 20 (44) | 19 (42) | 2 (4) | 13 (34) | 16 (42) | 7 (18) | 0 (0) | | | | |
| | urothelial hyperplasia:pelvis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 9

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|--|---------------------------------------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | Grade | | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | | | | |
| urin bladd | simple hyperplasia:transitional epithelium | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| pituitary | cyst | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | | | | |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | | | | |
| | hyperplasia | 14 | 1 | 0 | 0 | 11 | 1 | 0 | 0 | 6 | 3 | 0 | 0 * | 8 | 3 | 0 | 0 | | | | |
| | | (36) | (3) | (0) | (0) | (28) | (3) | (0) | (0) | (13) | (7) | (0) | (0) | (21) | (8) | (0) | (0) | | | | |
| | Rathke pouch | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | | | | |
| | | (3) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | | | | |
| thyroid | C-cell hyperplasia | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 8 | 3 | 0 | 0 | 6 | 0 | 0 | 0 | 5 | 2 | 0 | 0 | 6 | 2 | 0 | 0 | | | | |
| | | (21) | (8) | (0) | (0) | (15) | (0) | (0) | (0) | (11) | (4) | (0) | (0) | (16) | (5) | (0) | (0) | | | | |
| | focal follicular cell hyperplasia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 10

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|---------------------------|--|------|------|------|------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| parathyroid | cyst | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| adrenal | hyperplasia:cortical cell | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:medulla | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 7 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 * | 1 | 0 | 0 | 0 * | 0 | 0 | 0 | 0 |
| | | (18) | (3) | (0) | (0) | (5) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | focal fatty change:cortex | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 2 | 0 | 0 | 0 | 3 | 2 | 0 | 0 | 5 | 1 | 0 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (5) | (0) | (0) | (0) | (8) | (5) | (0) | (0) | (11) | (2) | (0) | (0) | (11) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| testis | atrophy | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 6 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 4 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (15) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (24) | (0) | (0) | (0) | (11) | (5) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 11

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|-------------------------------|---------------------------------------|-------|------|------|-------|------|------|------|-------|-------|------|------|-------|------|------|------|-------|-----|-----|-----|
| | | Grade | | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| testis | mineralization | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | | | | |
| | | (5) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | | | | |
| | arteritis | 2 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 11 | 2 | 0 | 0 * | 4 | 2 | 0 | 0 | | | | |
| | | (5) | (0) | (0) | (0) | (5) | (5) | (0) | (0) | (24) | (4) | (0) | (0) | (11) | (5) | (0) | (0) | | | | |
| | | | | | | | | | | | | | | | | | | | | | |
| | interstitial cell hyperplasia | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | | | | |
| | | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | | | | |
| | | | | | | | | | | | | | | | | | | | | | |
| semin ves | hyperplasia | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | | |
| prostate | inflammation | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 13 | 1 | 0 | 0 | 9 | 1 | 0 | 0 | 14 | 2 | 0 | 0 | 15 | 0 | 0 | 0 | | | | |
| | | (33) | (3) | (0) | (0) | (23) | (3) | (0) | (0) | (31) | (4) | (0) | (0) | (39) | (0) | (0) | (0) | | | | |
| | hyperplasia | 9 | 7 | 0 | 0 | 7 | 3 | 0 | 0 | 9 | 5 | 0 | 0 | 8 | 3 | 0 | 0 | | | | |
| | | (23) | (18) | (0) | (0) | (18) | (8) | (0) | (0) | (20) | (11) | (0) | (0) | (21) | (8) | (0) | (0) | | | | |
| | | | | | | | | | | | | | | | | | | | | | |
| mammary gl | galactoceles | <39> | | | | <39> | | | | <45> | | | | <38> | | | | | | | |
| | | 1 | 0 | 0 | 0 | 5 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | | | | |
| | | (3) | (0) | (0) | (0) | (13) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 12

| Organ | Findings | Group Name | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--------------------------|-------------------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | No. of Animals on Study | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | Grade | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | | |
| eye | cataract | | | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | | (3) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| | | | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | retinal atrophy | | | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | | (3) | (0) | (0) | (0) | (3) | (5) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (3) | (0) | (0) |
| Harder gl | degeneration | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | lymphocytic infiltration | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) |
| | hyperplasia | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | | |
| muscle | arteritis | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 13

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------------|----------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | | 39 | | | | 39 | | | | 45 | | | | 38 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | |
| bone | osteosclerosis | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Body cavities} | | | | | | | | | | | | | | | | | | |
| pleura | inflammation | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| mesenterium | arteritis | | <39> | | | | <39> | | | | <45> | | | | <38> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

(HPT150)

BAIS3

APPENDIX J 4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY,
RAT: FEMALE: ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 17

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--|---------------------------------------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | | | | |
| subcutis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | mineralization | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | squamous cell hyperplasia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 2 | 0 | 2 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (2) | (0) | (2) | (0) | (2) | (0) |
| | goblet cell hyperplasia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | 0 | 10 | 36 | 1 | 3 | 14 | 33 | 0 | 0 | 13 | 34 | 0 | 5 | 16 | 24 | 0 * | 10 | 32 | 48 | 0 |
| | | (0) | (20) | (72) | (2) | (6) | (28) | (66) | (0) | (0) | (26) | (68) | (0) | (10) | (32) | (48) | (0) | (10) | (32) | (48) | (0) |
| | eosinophilic change:respiratory epithelium | 7 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 14 | 0 | 0 | 0 |
| | | (14) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (14) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 18

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|---|---------------------------------------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|-------|-------|-------|-----|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation:foreign body | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 31 | 3 | 0 | 0 | 0 | 0 | 0 | ** |
| | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (62) | (6) | (0) | (0) | (0) | (0) | (0) | |
| | inflammation:respiratory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 17 | 0 | 0 | 0 | 24 | 9 | 3 | 0 | 0 | 0 | 0 | ** |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (34) | (0) | (0) | (0) | (48) | (18) | (6) | (0) | (0) | (0) | (0) | |
| | respiratory metaplasia:olfactory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | ** |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (26) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | squamous cell metaplasia:respiratory epithelium | 0 | 0 | 0 | 0 | 18 | 0 | 0 | 0 | 27 | 14 | 1 | 0 | 19 | 17 | 9 | 0 | 0 | 0 | 0 | ** |
| | | (0) | (0) | (0) | (0) | (36) | (0) | (0) | (0) | (54) | (28) | (2) | (0) | (38) | (34) | (18) | (0) | (0) | (0) | (0) | |
| | atrophy:olfactory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 5 | 0 | 0 | 0 | 0 | 0 | * |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (10) | (0) | (0) | (0) | (0) | (0) | |
| | necrosis:olfactory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (6) | (2) | (0) | (0) | (0) | (0) | (0) | |
| | hyperplasia:respiratory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 3 | 0 | 0 | 13 | 18 | 5 | 0 | 0 | 0 | 0 | ** |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (16) | (6) | (0) | (0) | (26) | (36) | (10) | (0) | (0) | (0) | (0) | |
| larynx | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 19

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|---------------------------------------|--|--------|--------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
| | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| lung | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (8) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | hemorrhage | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | edema | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammatory infiltration | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | osseous metaplasia | | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | accumulation of foamy cells | | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| | bronchiolar-alveolar cell hyperplasia | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (6) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | granulation | | 9 | 5 | 0 | 0 | 2 | 4 | 0 | 0 | 8 | 3 | 0 | 0 | 7 | 5 | 0 | 0 |
| | | | (18) | (10) | (0) | (0) | (4) | (8) | (0) | (0) | (16) | (6) | (0) | (0) | (14) | (10) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 20

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|------------------------------|--|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | increased hematopoiesis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| lymph node | lymphadenitis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (8) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| spleen | thrombus | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | deposit of hemosiderin | | 25 | 1 | 0 | 0 | 14 | 0 | 0 | 0 * | 17 | 0 | 0 | 0 | 18 | 2 | 0 | 0 |
| | | | (50) | (2) | (0) | (0) | (28) | (0) | (0) | (0) | (34) | (0) | (0) | (0) | (36) | (4) | (0) | (0) |
| | fibrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | | 7 | 1 | 2 | 0 | 7 | 1 | 0 | 0 | 3 | 1 | 4 | 1 | 4 | 1 | 1 | 0 |
| | | | (14) | (2) | (4) | (0) | (14) | (2) | (0) | (0) | (6) | (2) | (8) | (2) | (8) | (2) | (2) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | myocardial fibrosis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 26 | 0 | 0 | 0 | 28 | 0 | 0 | 0 | 27 | 0 | 0 | 0 | 26 | 0 | 0 | 0 |
| | | | (52) | (0) | (0) | (0) | (56) | (0) | (0) | (0) | (54) | (0) | (0) | (0) | (52) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 21

| Organ | Findings | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|-------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | Group Name | | | | 50 | | | | 50 | | | | 50 | | | |
| | | No. of Animals on Study | | | | Grade | | | | Grade | | | | Grade | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | |
| tooth | inflammation | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| tongue | arteritis | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| stomach | inflammatory infiltration | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:forestomach | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (0) | (0) | (0) |
| | hyperplasia:forestomach | 2 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (4) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| | erosion:glandular stomach | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| | ulcer:glandular stomach | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 22

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-----------------------|---------------------------------------|------|------|------|-------|------|------|------|-------|------|------|------|-------|-------|------|------|-------|-------|------|------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | | | | | |
| | herniation | <50> | | | | 7 | 0 | 0 | 0 | <50> | | | | 11 | 0 | 0 | 0 | <50> | | | |
| | | (14) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (22) | (0) | (0) | (0) | (16) | (0) | (0) | (0) |
| | necrosis:central | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | necrosis:focal | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | granulation | 18 | 1 | 2 | 0 | 10 | 4 | 1 | 0 | 21 | 0 | 1 | 0 | 12 | 5 | 0 | 0 | (24) | (10) | (0) | (0) |
| | | (36) | (2) | (4) | (0) | (20) | (8) | (2) | (0) | (42) | (0) | (2) | (0) | (24) | (10) | (0) | (0) | (24) | (10) | (0) | (0) |
| | clear cell focus | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | basophilic cell focus | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | (6) | (0) | (0) | (0) |
| | | (2) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| | vacuolated cell focus | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | bile duct hyperplasia | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | (4) | (0) | (0) | (0) |
| | | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 23

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|------------------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| liver | cholangiofibrosis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| pancreas | atrophy | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (2) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | islet cell hyperplasia | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | infarct | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyaline droplet | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 24

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-----------------------|---------------------------------------|-------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|-------|------|------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | | | | |
| kidney | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | chronic nephropathy | 12 | 2 | 2 | 0 | 11 | 3 | 3 | 0 | 12 | 2 | 2 | 0 | 5 | 1 | 2 | 0 | (24) | (4) | (4) | (0) |
| | | (24) | (4) | (4) | (0) | (22) | (6) | (6) | (0) | (24) | (4) | (4) | (0) | (10) | (2) | (4) | (0) | | | | |
| | hydronephrosis | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | (2) | (0) | (0) | (0) |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | | |
| | mineralization:pelvis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | (0) | (0) | (0) | (0) |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | | |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| pituitary | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | angiectasis | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | (0) | (0) | (0) | (0) |
| | | (0) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | | | | |
| | cyst | 11 | 6 | 0 | 0 | 9 | 1 | 1 | 0 | 10 | 1 | 0 | 0 | 12 | 2 | 0 | 0 | (22) | (12) | (0) | (0) |
| | | (22) | (12) | (0) | (0) | (18) | (2) | (2) | (0) | (20) | (2) | (0) | (0) | (24) | (4) | (0) | (0) | | | | |
| | hyperplasia | 5 | 2 | 0 | 0 | 7 | 2 | 0 | 0 | 6 | 4 | 0 | 0 | 7 | 1 | 0 | 0 | (10) | (4) | (0) | (0) |
| | | (10) | (4) | (0) | (0) | (14) | (4) | (0) | (0) | (12) | (8) | (0) | (0) | (14) | (2) | (0) | (0) | | | | |
| | Rathke pouch | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | (6) | (0) | (0) | (0) |
| | | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 25

| Organ | Findings | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-----------------------------------|---------------------------------------|--------|-------|-------|---------|-------|-------|-------|---------|-------|-------|-------|---------|-------|-------|-------|
| | | Group Name No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | | | | 1 2 3 4 | | | | 1 2 3 4 | | | | 1 2 3 4 | | | |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | |
| thyroid | | | | | | | | | | | | | | | | | |
| | ultimibranhial body remanet | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | C-cell hyperplasia | 6 | 8 | 0 | 0 | 7 | 0 | 0 | 0 * | 8 | 1 | 0 | 0 * | 7 | 2 | 0 | 0 |
| | | (12) | (16) | (0) | (0) | (14) | (0) | (0) | (0) | (16) | (2) | (0) | (0) | (14) | (4) | (0) | (0) |
| | focal follicular cell hyperplasia | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| adrenal | | | | | | | | | | | | | | | | | |
| | hemorrhage | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | peliosis-like lesion | 32 | 0 | 0 | 0 | 27 | 0 | 0 | 0 | 26 | 0 | 0 | 0 | 23 | 0 | 0 | 0 |
| | | (64) | (0) | (0) | (0) | (54) | (0) | (0) | (0) | (52) | (0) | (0) | (0) | (46) | (0) | (0) | (0) |
| | necrosis:zonal | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:cortical cell | 5 | 1 | 0 | 0 | 7 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 5 | 1 | 0 | 0 |
| | | (10) | (2) | (0) | (0) | (14) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (10) | (2) | (0) | (0) |
| | focal fatty change:cortex | 5 | 4 | 0 | 0 | 2 | 0 | 2 | 0 | 7 | 1 | 0 | 0 | 7 | 0 | 0 | 0 |
| | | (10) | (8) | (0) | (0) | (4) | (0) | (4) | (0) | (14) | (2) | (0) | (0) | (14) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 26

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|--------------------------------|---------------------------------------|-------|-------|-------|--------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| ovary | cyst | <50> | | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| uterus | decidual change | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | cystic endometrial hyperplasia | 1 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (2) | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| mammary gl | duct ectasia | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | galactoceles | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| {Nervous system} | | | | | | | | | | | | | | | | | | | | | |
| brain | hemorrhage | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (2) | (2) | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) |

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 < a > a : Number of animals examined at the site
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 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 27

| | | Group Name | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--------------------|-------------------------|-------|-------|-------|-------|--------|--------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Organ_____ | Findings_____ | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| | | | | | | | | | | | | | | | | | | |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| brain | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | granulation | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | gliosis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spinal cord | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hemorrhage | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | radiculoneuropathy | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| eye | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cataract | | 2 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | retinal atrophy | | 1 | 1 | 0 | 0 | 0 | 5 | 3 | 0 | 2 | 3 | 1 | 0 | 1 | 3 | 0 | 0 |
| | | | (2) | (2) | (0) | (0) | (0) | (10) | (6) | (0) | (4) | (6) | (2) | (0) | (2) | (6) | (0) | (0) |

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 < a > a : Number of animals examined at the site
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STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 28

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--------------------------|---------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | | | | |
| Harder gl | degeneration | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | lymphocytic infiltration | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | | | | |
| muscle | atrophy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| bone | osteodystrophy | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | osteosclerosis | 4 | 2 | 0 | 0 | 3 | 4 | 0 | 0 | 3 | 2 | 0 | 0 | 4 | 6 | 0 | 0 | 4 | 6 | 0 | 0 |
| | | (8) | (4) | (0) | (0) | (6) | (8) | (0) | (0) | (6) | (4) | (0) | (0) | (8) | (12) | (0) | (0) | (8) | (12) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 29

| Organ | Findings | Group Name | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-------|----------|-------------------------|-----|-----|-----|------|-----|-----|-----|------|-----|-----|-----|------|-----|-----|-----|-------|--|--|--|
| | | No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | | | |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | | | |

{Body cavities}

| adipose | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
|-------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| granulation | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

(HPT150)

BAIS3

APPENDIX J 5

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY,
RAT: FEMALE: DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 12

| | | Group Name | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|---|-------------------------|-------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|
| | | No. of Animals on Study | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | |
| subcutis | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | inflammation | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | thrombus | | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | | 0 | 3 | 5 | 0 | 1 | 3 | 8 | 0 | 0 | 3 | 5 | 0 | 2 | 3 | 2 | 0 |
| | | | (0) | (27) | (45) | (0) | (8) | (25) | (67) | (0) | (0) | (30) | (50) | (0) | (20) | (30) | (20) | (0) |
| | eosinophilic change:respiratory epithelium | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation:foreign body | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 7 | 0 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (70) | (0) | (0) | (0) |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 * | 5 | 2 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (50) | (0) | (0) | (0) | (50) | (20) | (0) | (0) |
| | respiratory metaplasia:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 13

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|---|--|-------------|------------|------------|------------|-------------|------------|------------|------------|-------------|-------------|-------------|---------------|-------------|-------------|-------------|---------------|
| | | | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | squamous cell metaplasia:respiratory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 4 (40) | 2 (20) | 1 (10) | 0 ** (0) | 5 (50) | 4 (40) | 1 (10) | 0 ** (0) |
| | atrophy:olfactory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 4 (40) | 0 (0) | 0 (0) |
| | necrosis:olfactory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (10) | 0 (0) | 0 (0) | 0 (0) | 1 (10) | 1 (10) | 0 (0) | 0 (0) |
| | hyperplasia:respiratory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 5 (50) | 1 (10) | 0 (0) | 0 ** (0) | 3 (30) | 3 (30) | 3 (30) | 0 ** (0) |
| larynx | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | inflammation | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| lung | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | congestion | | 4 (36) | 0 (0) | 0 (0) | 0 (0) | 3 (25) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (20) | 0 (0) | 0 (0) | 0 (0) |
| | hemorrhage | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (10) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 14

| | | Group Name | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|-----------------------------|-------------------------|--------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| Organ_____ | Findings_____ | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| lung | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | edema | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | osseous metaplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | accumulation of foamy cells | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | granulation | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | increased hematopoiesis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| spleen | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | thrombus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 15

| | | Group Name | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|------------------------------|-------------------------|-------|------|------|------|-------|------|------|------|-------|-------|-------|-------|-------|-------|-------|------|
| | | No. of Animals on Study | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| spleen | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | deposit of hemosiderin | | 5 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (45) | (9) | (0) | (0) | (25) | (0) | (0) | (0) | (30) | (0) | (0) | (0) | (10) | (20) | (0) | (0) |
| | extramedullary hematopoiesis | | 0 | 0 | 1 | 0 | 3 | 1 | 0 | 0 | 1 | 0 | 3 | 1 | 0 | 1 | 1 | 0 |
| | | | (0) | (0) | (9) | (0) | (25) | (8) | (0) | (0) | (10) | (0) | (30) | (10) | (0) | (10) | (10) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | myocardial fibrosis | | 5 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 5 | 0 | 0 | 0 |
| | | | (45) | (0) | (0) | (0) | (33) | (0) | (0) | (0) | (30) | (0) | (0) | (0) | (50) | (0) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| stomach | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | inflammatory infiltration | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:forestomach | | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (9) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (10) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 16

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|---------------------------------------|------|------|------|-------|------|------|------|-------|------|------|------|-------|-------|------|------|-------|-------|------|------|
| | | Grade | | | | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| stomach | | <11> | | | | <12> | | | | <10> | | | | <10> | | | | <10> | | | |
| | hyperplasia:forestomach | 2 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (18) | (9) | (0) | (0) | (17) | (0) | (0) | (0) | (30) | (0) | (0) | (0) | (30) | (0) | (0) | (0) | (30) | (0) | (0) | (0) |
| | erosion:glandular stomach | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | ulcer:glandular stomach | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| liver | | <11> | | | | <12> | | | | <10> | | | | <10> | | | | <10> | | | |
| | herniation | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (33) | (0) | (0) | (0) | (40) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | necrosis:central | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (8) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | necrosis:focal | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | granulation | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) |
| | bile duct hyperplasia | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 17

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|------------------------|---------------------------------------|-------|-------|-------|--------|-------|-------|-------|--------|--------|--------|-------|--------|--------|--------|--------|--------|-------|-------|-------|
| | | Grade | | | | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| pancreas | | <11> | | | | <12> | | | | <10> | | | | <10> | | | | <10> | | | |
| | atrophy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | islet cell hyperplasia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | | | | |
| kidney | | <11> | | | | <12> | | | | <10> | | | | <10> | | | | <10> | | | |
| | infarct | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | chronic nephropathy | 0 | 0 | 1 | 0 | 2 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 0 |
| | | (0) | (0) | (9) | (0) | (17) | (0) | (8) | (0) | (10) | (0) | (10) | (0) | (10) | (0) | (10) | (10) | (10) | (0) | (0) | (0) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| pituitary | | <11> | | | | <12> | | | | <10> | | | | <10> | | | | <10> | | | |
| | angiectasis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 18

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|--|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| | | | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | cyst | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | | | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (27) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | hyperplasia | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | Rathke pouch | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| thyroid | C-cell hyperplasia | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| adrenal | peliosis-like lesion | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | | | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (36) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | hyperplasia:cortical cell | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | focal fatty change:cortex | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 19

| | | Group Name | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|--------------------|-------------------------|-------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| Organ_____ | Findings_____ | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| ovary | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | cyst | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| mammary gl | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | galactoceles | | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (9) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (20) | (0) | (0) | (0) |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | hemorrhage | | 1 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (9) | (9) | (0) | (0) | (17) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) |
| | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | granulation | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spinal cord | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | hemorrhage | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | radiculoneuropathy | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 20

| Organ | Findings | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|-----------------|-------|--------|-------|-------|-------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | 11 | | | | 12 | | | | 10 | | | | 10 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | |
| eye | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | cataract | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | retinal atrophy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (10) | (0) | (0) | (0) | (10) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | |
| muscle | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | atrophy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| bone | | <11> | | | | <12> | | | | <10> | | | | <10> | | | |
| | osteodystrophy | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | osteosclerosis | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (18) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

APPENDIX J 6

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY,
RAT: FEMALE: SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 14

| Organ | Findings | Group Name No. of Animals on Study Grade | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | | | |
|----------------------|---|--|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|--------|--------|--------|-------|-----|-----|-----|
| | | | 39 | | | | 38 | | | | 40 | | | | 40 | | | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | | |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | | |
| | mineralization | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | | | |
| | squamous cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (3) | (0) | | | |
| | goblet cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | | | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | | | |
| | eosinophilic change:olfactory epithelium | | 0 | 7 | 31 | 1 | 2 | 11 | 25 | 0 | 0 | 10 | 29 | 3 | 13 | 22 | 0 | | | |
| | | | (0) | (18) | (79) | (3) | (5) | (29) | (66) | (0) | (0) | (25) | (73) | (8) | (33) | (55) | (0) | | | |
| | eosinophilic change:respiratory epithelium | | 6 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 6 | 0 | 0 | 7 | 0 | 0 | 0 | | | |
| | | | (15) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | (15) | (0) | (0) | (18) | (0) | (0) | (0) | | | |
| | inflammation:foreign body | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 24 | 3 | 0 | 0 ** | | | |
| | | | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (60) | (8) | (0) | (0) | | | |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 0 | 0 | 19 | 7 | 3 | 0 ** | | | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (30) | (0) | (0) | (48) | (18) | (8) | (0) | | | |
| | respiratory metaplasia:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 0 | 0 | 0 ** | | | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (30) | (0) | (0) | (0) | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 15

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------|---|--|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|-------|-----|-----|-----|
| | | 39 | | | | 38 | | | | 40 | | | | 40 | | | | 40 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | squamous cell metaplasia:respiratory epithelium | 0 | 0 | 0 | 0 | 17 | 0 | 0 | 0 ** | 23 | 12 | 0 | 0 ** | 14 | 13 | 8 | 0 ** | | | | |
| | | (0) | (0) | (0) | (0) | (45) | (0) | (0) | (0) | (58) | (30) | (0) | (0) | (35) | (33) | (20) | (0) | | | | |
| | atrophy:olfactory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | | | | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (5) | (3) | (0) | (0) | | | | |
| | necrosis:olfactory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | | | | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | | | | |
| | hyperplasia:respiratory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 2 | 0 | 0 | 10 | 15 | 2 | 0 ** | | | | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (5) | (0) | (0) | (25) | (38) | (5) | (0) | | | | |
| larynx | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | inflammation | 5 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | | | | |
| | | (13) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | | | | |
| lung | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | hemorrhage | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | | |
| | inflammatory infiltration | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | | | | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 16

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|---------------------------------------|--|-------|-------|------|------|-------|-------|------|------|-------|------|------|------|-------|-------|------|------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| lung | | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | osseous metaplasia | | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | accumulation of foamy cells | | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (5) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | bronchiolar-alveolar cell hyperplasia | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (8) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | granulation | | 7 | 5 | 0 | 0 | 2 | 4 | 0 | 0 | 7 | 3 | 0 | 0 | 7 | 5 | 0 | 0 |
| | | | (18) | (13) | (0) | (0) | (5) | (11) | (0) | (0) | (18) | (8) | (0) | (0) | (18) | (13) | (0) | (0) |
| lymph node | | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | lymphadenitis | | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (10) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| spleen | | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | deposit of hemosiderin | | 20 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 14 | 0 | 0 | 0 | 17 | 0 | 0 | 0 |
| | | | (51) | (0) | (0) | (0) | (29) | (0) | (0) | (0) | (35) | (0) | (0) | (0) | (43) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 17

| Organ | Findings | Group Name No. of Animals on Study | | | | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|------------------------|------------------------------|---------------------------------------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | Grade | | | | 39 | | | | 38 | | | | 40 | | | | 40 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | | | | |
| spleen | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | fibrosis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | 7 | 1 | 1 | 0 | 4 | 0 | 0 | 0 | 2 | 1 | 1 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (18) | (3) | (3) | (0) | (11) | (0) | (0) | (0) | (5) | (3) | (3) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | | | | |
| heart | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | myocardial fibrosis | 21 | 0 | 0 | 0 | 24 | 0 | 0 | 0 | 24 | 0 | 0 | 0 | 21 | 0 | 0 | 0 | 21 | 0 | 0 | 0 |
| | | (54) | (0) | (0) | (0) | (63) | (0) | (0) | (0) | (60) | (0) | (0) | (0) | (53) | (0) | (0) | (0) | (53) | (0) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| tooth | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | inflammation | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| tongue | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | arteritis | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 18

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|---------------------------|---------------------------------------|------|------|------|-------|------|------|------|-------|------|------|------|-------|-------|------|------|-------|-------|------|------|
| | | Grade | | | | 39 | | | | 38 | | | | 40 | | | | 40 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| stomach | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | erosion:glandular stomach | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| liver | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | herniation | 7 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 6 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (15) | (0) | (0) | (0) | (15) | (0) | (0) | (0) |
| | granulation | 17 | 1 | 2 | 0 | 10 | 3 | 1 | 0 | 19 | 0 | 1 | 0 | 12 | 4 | 0 | 0 | 12 | 4 | 0 | 0 |
| | | (44) | (3) | (5) | (0) | (26) | (8) | (3) | (0) | (48) | (0) | (3) | (0) | (30) | (10) | (0) | (0) | (30) | (10) | (0) | (0) |
| | clear cell focus | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | basophilic cell focus | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | vacuolated cell focus | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) |
| | bile duct hyperplasia | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | cholangiofibrosis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 19

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|------------------------|---------------------------------------|------------|------------|------------|-------------|------------|------------|------------|--------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|
| | | Grade | | | | 39 | | | | 38 | | | | 40 | | | | 40 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| pancreas | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | atrophy | 1 (3) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| | islet cell hyperplasia | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | | | | |
| kidney | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | infarct | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | hyaline droplet | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | chronic nephropathy | 12 (31) | 2 (5) | 1 (3) | 0 (0) | 9 (24) | 3 (8) | 2 (5) | 0 (0) | 11 (28) | 2 (5) | 1 (3) | 0 (0) | 4 (10) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | hydronephrosis | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | mineralization:pelvis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 20

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|--------------------|-----------------------------------|---------------------------------------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | Grade | | | | 39 | | | | 38 | | | | 40 | | | | 40 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| pituitary | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | angiectasis | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (3) | (0) | (0) |
| | cyst | 8 | 6 | 0 | 0 | 6 | 1 | 1 | 0 | 9 | 1 | 0 | 0 | 10 | 2 | 0 | 0 | 10 | 2 | 0 | 0 |
| | | (21) | (15) | (0) | (0) | (16) | (3) | (3) | (0) | (23) | (3) | (0) | (0) | (25) | (5) | (0) | (0) | (25) | (5) | (0) | (0) |
| | hyperplasia | 5 | 2 | 0 | 0 | 5 | 2 | 0 | 0 | 6 | 4 | 0 | 0 | 7 | 1 | 0 | 0 | 7 | 1 | 0 | 0 |
| | | (13) | (5) | (0) | (0) | (13) | (5) | (0) | (0) | (15) | (10) | (0) | (0) | (18) | (3) | (0) | (0) | (18) | (3) | (0) | (0) |
| | Rathke pouch | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| thyroid | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | ultimibranhial body remanet | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | C-cell hyperplasia | 6 | 8 | 0 | 0 | 5 | 0 | 0 | 0 * | 6 | 1 | 0 | 0 * | 7 | 2 | 0 | 0 | 7 | 2 | 0 | 0 |
| | | (15) | (21) | (0) | (0) | (13) | (0) | (0) | (0) | (15) | (3) | (0) | (0) | (18) | (5) | (0) | (0) | (18) | (5) | (0) | (0) |
| | focal follicular cell hyperplasia | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| adrenal | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | hemorrhage | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 21

| Organ | Findings | Group Name No. of Animals on Study | | | | Oppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|-----------------------|---------------------------|---------------------------------------|------------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| | | Grade | | | | 39 | | | | 38 | | | | 40 | | | | 40 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| adrenal | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | peliosis-like lesion | 28 (72) | 0 (0) | 0 (0) | 0 (0) | 24 (63) | 0 (0) | 0 (0) | 0 (0) | 24 (60) | 0 (0) | 0 (0) | 0 (0) | 22 (55) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | necrosis:zonal | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | hyperplasia:cortical cell | 5 (13) | 1 (3) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 (0) | 5 (13) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | focal fatty change:cortex | 4 (10) | 4 (10) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 2 (5) | 0 (0) | 7 (18) | 1 (3) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| ovary | | <39> | | | | <37> | | | | <40> | | | | <40> | | | | <40> | | | |
| | cyst | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| uterus | | <39> | | | | <38> | | | | <40> | | | | <40> | | | | <40> | | | |
| | decidual change | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 22

| Organ | Findings | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--------------------------------|-------------------------|-------|-------|-------|--------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | | Group Name | | | | 39 | | | | 38 | | | | 40 | | | |
| | | No. of Animals on Study | | | | Grade | | | | 1 | | | | 2 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | |
| uterus | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | cystic endometrial hyperplasia | 1 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (3) | (5) | (0) | (0) | (0) | (8) | (0) | (0) | (3) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| mammary gl | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | duct ectasia | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | galactoceles | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| {Nervous system} | | | | | | | | | | | | | | | | | |
| brain | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | hemorrhage | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | gliosis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | |
| eye | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | cataract | 2 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (5) | (0) | (0) | (0) | (21) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 23

| Organ | Findings | Group Name No. of Animals on Study Grade | 0ppm | | | | 3ppm | | | | 6ppm | | | | 12ppm | | | |
|----------------------------------|--------------------------|--|--------|-------|-------|-------|-------|--------|-------|-------|-------|-------|-------|-------|--------|--------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | retinal atrophy | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | | | 1 | 1 | 0 | 0 | 0 | 5 | 3 | 0 | 1 | 2 | 1 | 0 | 1 | 2 | 0 | 0 |
| | | | (3) | (3) | (0) | (0) | (0) | (13) | (8) | (0) | (3) | (5) | (3) | (0) | (3) | (5) | (0) | (0) |
| Harder gl | degeneration | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | lymphocytic infiltration | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | |
| bone | osteosclerosis | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | | | 4 | 0 | 0 | 0 | 3 | 4 | 0 | 0 | 3 | 2 | 0 | 0 | 4 | 5 | 0 | 0 |
| | | | (10) | (0) | (0) | (0) | (8) | (11) | (0) | (0) | (8) | (5) | (0) | (0) | (10) | (13) | (0) | (0) |
| {Body cavities} | | | | | | | | | | | | | | | | | | |
| adipose | granulation | | <39> | | | | <38> | | | | <40> | | | | <40> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

APPENDIX K 1

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED
RAT: MALE
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 1

| Time-related Weeks | Items | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--------------------|-------------------------------------|------------|------|------|------|-------|
| 0 - 52 | NO. OF EXAMINED ANIMALS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF TOTAL TUMORS | | 0 | 0 | 0 | 0 |
| 53 - 78 | NO. OF EXAMINED ANIMALS | | 1 | 0 | 0 | 3 |
| | NO. OF ANIMALS WITH TUMORS | | 1 | 0 | 0 | 3 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 0 | 0 | 2 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 1 | 0 | 0 | 1 |
| | NO. OF BENIGN TUMORS | | 1 | 0 | 0 | 3 |
| | NO. OF MALIGNANT TUMORS | | 1 | 0 | 0 | 1 |
| | NO. OF TOTAL TUMORS | | 2 | 0 | 0 | 4 |
| 79 - 104 | NO. OF EXAMINED ANIMALS | | 10 | 11 | 5 | 9 |
| | NO. OF ANIMALS WITH TUMORS | | 10 | 11 | 5 | 9 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 4 | 3 | 0 | 3 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 6 | 8 | 5 | 6 |
| | NO. OF BENIGN TUMORS | | 15 | 16 | 11 | 13 |
| | NO. OF MALIGNANT TUMORS | | 6 | 6 | 3 | 7 |
| | NO. OF TOTAL TUMORS | | 21 | 22 | 14 | 20 |
| 105 - 105 | NO. OF EXAMINED ANIMALS | | 39 | 39 | 45 | 38 |
| | NO. OF ANIMALS WITH TUMORS | | 39 | 39 | 45 | 38 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 13 | 12 | 18 | 16 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 26 | 27 | 27 | 22 |
| | NO. OF BENIGN TUMORS | | 71 | 78 | 73 | 67 |
| | NO. OF MALIGNANT TUMORS | | 5 | 5 | 5 | 4 |
| | NO. OF TOTAL TUMORS | | 76 | 83 | 78 | 71 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 2

| Time-related Weeks | Items | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|-----------------------|-------------------------------------|------------|------|------|------|-------|
| 0 - 105 | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 17 | 15 | 18 | 21 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 33 | 35 | 32 | 29 |
| | NO. OF BENIGN TUMORS | | 87 | 94 | 84 | 83 |
| | NO. OF MALIGNANT TUMORS | | 12 | 11 | 8 | 12 |
| | NO. OF TOTAL TUMORS | | 99 | 105 | 92 | 95 |

(HPT070)

BAIS3

APPENDIX K 2

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED
RAT: FEMALE
(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 3

| Time-related Weeks | Items | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|-----------------------|-------------------------------------|------------|------|------|------|-------|
| 0 - 52 | NO. OF EXAMINED ANIMALS | | 1 | 0 | 0 | 1 |
| | NO. OF ANIMALS WITH TUMORS | | 1 | 0 | 0 | 1 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 0 | 0 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 1 | 0 | 0 | 1 |
| | NO. OF TOTAL TUMORS | | 1 | 0 | 0 | 1 |
| 53 - 78 | NO. OF EXAMINED ANIMALS | | 2 | 2 | 1 | 0 |
| | NO. OF ANIMALS WITH TUMORS | | 1 | 2 | 1 | 0 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 1 | 1 | 0 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 1 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 1 | 1 | 1 | 0 |
| | NO. OF MALIGNANT TUMORS | | 0 | 2 | 0 | 0 |
| | NO. OF TOTAL TUMORS | | 1 | 3 | 1 | 0 |
| 79 - 104 | NO. OF EXAMINED ANIMALS | | 8 | 10 | 9 | 9 |
| | NO. OF ANIMALS WITH TUMORS | | 8 | 10 | 8 | 9 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 5 | 7 | 5 | 5 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 3 | 3 | 3 | 4 |
| | NO. OF BENIGN TUMORS | | 8 | 10 | 6 | 8 |
| | NO. OF MALIGNANT TUMORS | | 4 | 4 | 6 | 6 |
| | NO. OF TOTAL TUMORS | | 12 | 14 | 12 | 14 |
| 105 - 105 | NO. OF EXAMINED ANIMALS | | 39 | 38 | 40 | 40 |
| | NO. OF ANIMALS WITH TUMORS | | 25 | 29 | 25 | 25 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 10 | 14 | 20 | 16 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 15 | 15 | 5 | 9 |
| | NO. OF BENIGN TUMORS | | 38 | 45 | 28 | 35 |
| | NO. OF MALIGNANT TUMORS | | 4 | 5 | 5 | 2 |
| | NO. OF TOTAL TUMORS | | 42 | 50 | 33 | 37 |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrJ
REPORT TYPE : A1
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 4

| Time-related Weeks | Items | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|-----------------------|-------------------------------------|------------|------|------|------|-------|
| 0 - 105 | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 35 | 41 | 34 | 35 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 17 | 22 | 26 | 22 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 18 | 19 | 8 | 13 |
| | NO. OF BENIGN TUMORS | | 47 | 56 | 35 | 43 |
| | NO. OF MALIGNANT TUMORS | | 9 | 11 | 11 | 9 |
| | NO. OF TOTAL TUMORS | | 56 | 67 | 46 | 52 |

(HPT070)

BAIS3

APPENDIX L 1

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS: SUMMARY,
RAT: MALE: ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|----------------------------------|------------------------------|---------------------------------------|------------|------------|------------|-------------|
| {Integumentary system/appandage} | | | | | | |
| skin/app | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 1 (2%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | trichoepithelioma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| | basal cell epithelioma | | 1 (2%) | 0 (0%) | 0 (0%) | 1 (2%) |
| subcutis | keratoacanthoma | | 1 (2%) | 2 (4%) | 1 (2%) | 0 (0%) |
| | | | <50> | <50> | <50> | <50> |
| | fibroma | | 5 (10%) | 4 (8%) | 2 (4%) | 5 (10%) |
| | lipoma | | 1 (2%) | 1 (2%) | 0 (0%) | 1 (2%) |
| | hemangioma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | leiomyosarcoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | schwannoma:malignant | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| {Respiratory system} | | | | | | |
| nasal cavit | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 1 (2%) | 1 (2%) | 2 (4%) |
| lung | rhabdomyosarcoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| | bronchiolar-alveolar adenoma | | <50> | <50> | <50> | <50> |
| | | | 2 (4%) | 0 (0%) | 2 (4%) | 2 (4%) |

< a > a : Number of animals examined at the site
 b (c) b : Number of animals with neoplasm c : b / a * 100

(HPT085)

BAIS3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 2

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|------------------------|--------------------------------|---------------------------------------|-----------------|------------------|-----------------|------------------|
| {Respiratory system} | | | | | | |
| lung | bronchiolar-alveolar carcinoma | | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| {Hematopoietic system} | | | | | | |
| bone marrow | histiocytic sarcoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| spleen | mononuclear cell leukemia | | <50> 2 (4%) | <50> 5 (10%) | <50> 3 (6%) | <50> 7 (14%) |
| {Digestive system} | | | | | | |
| tongue | squamous cell papilloma | | <50> 0 (0%) | <49> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| salivary gl | adenocarcinoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| small intes | adenoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| | leiomyoma | | 0 (0%) | 2 (4%) | 0 (0%) | 0 (0%) |
| liver | hepatocellular adenoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| | cholangiocellular adenoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | histiocytic sarcoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| | hepatocellular carcinoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |

< a > a : Number of animals examined at the site
 b (c) b : Number of animals with neoplasm c : b / a * 100

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|--------------------|-----------------------------|---------------------------------------|-------------------|-------------------|-------------------|-------------------|
| {Digestive system} | | | | | | |
| pancreas | islet cell adenoma | | <50> 2 (4%) | <50> 2 (4%) | <50> 1 (2%) | <50> 3 (6%) |
| | islet cell adenocarcinoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| {Urinary system} | | | | | | |
| urin bladd | transitional cell papilloma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| {Endocrine system} | | | | | | |
| pituitary | adenoma | | <49> 14 (29%) | <50> 18 (36%) | <50> 18 (36%) | <50> 22 (44%) |
| | adenocarcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| thyroid | C-cell adenoma | | <50> 8 (16%) | <49> 10 (20%) | <50> 10 (20%) | <50> 5 (10%) |
| | follicular adenoma | | 1 (2%) | 3 (6%) | 0 (0%) | 1 (2%) |
| | C-cell carcinoma | | 3 (6%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | follicular adenocarcinoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| adrenal | pheochromocytoma | | <50> 5 (10%) | <50> 6 (12%) | <50> 3 (6%) | <50> 2 (4%) |
| | pheochromocytoma:malignant | | 1 (2%) | 0 (0%) | 1 (2%) | 1 (2%) |

< a > a : Number of animals examined at the site
 b (c) b : Number of animals with neoplasm c : b / a * 100

(HPT085)

BAIS3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|----------------------------------|-------------------------|---------------------------------------|------------|------------|------------|-------------|
| {Reproductive system} | | | | | | |
| testis | | | <50> | <50> | <50> | <50> |
| | interstitial cell tumor | | 41 (82%) | 42 (84%) | 42 (84%) | 37 (74%) |
| mammary gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | fibroadenoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| prep/cli gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 1 (2%) | 1 (2%) | 0 (0%) | 0 (0%) |
| {Special sense organs/appendage} | | | | | | |
| Zymbal gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 1 (2%) | 1 (2%) | 0 (0%) |
| | squamous cell carcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| {Body cavities} | | | | | | |
| peritoneum | | | <50> | <50> | <50> | <50> |
| | mesothelioma | | 0 (0%) | 3 (6%) | 1 (2%) | 1 (2%) |

< a > a : Number of animals examined at the site
 b (c) b : Number of animals with neoplasm c : b / a * 100

(HPT085)

BAIS3

APPENDIX L 2

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS: SUMMARY,
RAT: FEMALE: ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 5

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|----------------------------------|--------------------------------|---------------------------------------|------------|------------|------------|-------------|
| {Integumentary system/appandage} | | | | | | |
| skin/app | | | <50> | <50> | <50> | <50> |
| | trichoepithelioma | | 0 (0%) | 2 (4%) | 1 (2%) | 0 (0%) |
| | keratoacanthoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| subcutis | | | <50> | <50> | <50> | <50> |
| | fibroma | | 0 (0%) | 3 (6%) | 1 (2%) | 2 (4%) |
| | schwannoma:malignant | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | histiocytic sarcoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| {Respiratory system} | | | | | | |
| nasal cavit | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| lung | | | <50> | <50> | <50> | <50> |
| | bronchiolar-alveolar adenoma | | 1 (2%) | 0 (0%) | 1 (2%) | 1 (2%) |
| | bronchiolar-alveolar carcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| {Hematopoietic system} | | | | | | |
| thymus | | | <50> | <50> | <50> | <50> |
| | thymoma:benign | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| spleen | | | <50> | <50> | <50> | <50> |
| | mononuclear cell leukemia | | 5 (10%) | 9 (18%) | 3 (6%) | 4 (8%) |
| {Digestive system} | | | | | | |
| stomach | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 6

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|--------------------|-----------------------------|---------------------------------------|-------------------|-------------------|-------------------|-------------------|
| {Digestive system} | | | | | | |
| small intes | leiomyoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| liver | histiocytic sarcoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| pancreas | islet cell adenoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| | islet cell adenocarcinoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| {Urinary system} | | | | | | |
| kidney | lipoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| urin bladd | transitional cell papilloma | | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) | <50> 2 (4%) |
| {Endocrine system} | | | | | | |
| pituitary | adenoma | | <50> 18 (36%) | <50> 20 (40%) | <50> 18 (36%) | <50> 18 (36%) |
| | adenocarcinoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 2 (4%) | <50> 1 (2%) |
| thyroid | C-cell adenoma | | <50> 8 (16%) | <50> 6 (12%) | <50> 2 (4%) | <50> 5 (10%) |
| | follicular adenoma | | <50> 0 (0%) | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) |
| adrenal | pheochromocytoma | | <50> 1 (2%) | <50> 4 (8%) | <50> 0 (0%) | <50> 1 (2%) |

< a > a : Number of animals examined at the site
 b (c) b : Number of animals with neoplasm c : b / a * 100

(HPT085)

BAIS3

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|-----------------------|-----------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Endocrine system} | | | | | | |
| adrenal | cortical adenoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| {Reproductive system} | | | | | | |
| ovary | granulosa-theca cell tumor | | <50> 0 (0%) | <49> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| uterus | leiomyoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| | papillary adenoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| | endometrial stromal polyp | | 6 (12%) | 7 (14%) | 6 (12%) | 4 (8%) |
| | adenocarcinoma | | 2 (4%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | endometrial stromal sarcoma | | 1 (2%) | 0 (0%) | 2 (4%) | 2 (4%) |
| mammary gl | adenoma | | <50> 1 (2%) | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) |
| | fibroadenoma | | 6 (12%) | 5 (10%) | 3 (6%) | 5 (10%) |
| | adenocarcinoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| prep/cli gl | adenoma | | <50> 3 (6%) | <50> 2 (4%) | <50> 0 (0%) | <50> 1 (2%) |
| {Nervous system} | | | | | | |
| brain | histiocytic sarcoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |

< a > a : Number of animals examined at the site
 b (c) b : Number of animals with neoplasm c : b / a * 100

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

PAGE : 8

| Organ | Findings | Group Name No. of animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|-------|----------|---------------------------------------|------------|------------|------------|-------------|
|-------|----------|---------------------------------------|------------|------------|------------|-------------|

{Musculoskeletal system}

| | | | | | | |
|------|--------------|--|---------|---------|---------|---------|
| bone | | | <50> | <50> | <50> | <50> |
| | osteosarcoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |

| | | |
|---------|--|-----------------|
| < a > | a : Number of animals examined at the site | |
| b (c) | b : Number of animals with neoplasm | c : b / a * 100 |

(HPT085)

BAIS3

APPENDIX M 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANALYSIS, RAT: MALE

(2-YEAR STUDY)

STUDY No. : 0318
ANIMAL : RAT F344/DuCrJ
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|--------------|-------------|------------|-------------|
| SITE : subcutis TUMOR : fibroma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50(10.0) | 4/50(8.0) | 2/50(4.0) | 5/50(10.0) |
| Adjusted rates(b) | 10.20 | 7.14 | 2.22 | 8.89 |
| Terminal rates(c) | 3/39(7.7) | 2/39(5.1) | 1/45(2.2) | 2/38(5.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.2439 | | | |
| Prevalence method(d) | P = 0.5985 | | | |
| Combined analysis(d) | P = 0.4650 | | | |
| Cochran-Armitage test(e) | P = 1.0000 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.2180 | P = 0.3703 |
| SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50(8.0) | 0/50(0.0) | 2/50(4.0) | 2/50(4.0) |
| Adjusted rates(b) | 5.13 | 0.0 | 4.44 | 5.26 |
| Terminal rates(c) | 2/39(5.1) | 0/39(0.0) | 2/45(4.4) | 2/38(5.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9774 ? | | | |
| Prevalence method(d) | P = 0.3261 | | | |
| Combined analysis(d) | P = 0.6732 | | | |
| Cochran-Armitage test(e) | P = 0.6256 | | | |
| Fisher Exact test(e) | | P = 0.0587 | P = 0.3389 | P = 0.3389 |
| SITE : spleen TUMOR : mononuclear cell leukemia | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 5/50(10.0) | 3/50(6.0) | 7/50(14.0) |
| Adjusted rates(b) | 2.56 | 5.13 | 2.22 | 7.89 |
| Terminal rates(c) | 1/39(2.6) | 2/39(5.1) | 1/45(2.2) | 3/38(7.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1187 | | | |
| Prevalence method(d) | P = 0.1608 | | | |
| Combined analysis(d) | P = 0.0616 | | | |
| Cochran-Armitage test(e) | P = 0.1128 | | | |
| Fisher Exact test(e) | | P = 0.2180 | P = 0.5000 | P = 0.0798 |

STUDY No. : 0318
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : pancreas TUMOR : islet cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 2/50(4.0) | 1/50(2.0) | 3/50(6.0) |
| Adjusted rates(b) | 5.13 | 4.76 | 2.13 | 7.89 |
| Terminal rates(c) | 2/39(5.1) | 1/39(2.6) | 0/45(0.0) | 3/38(7.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.3018 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.6256 | | | |
| Fisher Exact test(e) | | P = 0.3087 | P = 0.5000 | P = 0.5000 |
| SITE : pituitary gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 14/49(28.6) | 18/50(36.0) | 18/50(36.0) | 22/50(44.0) |
| Adjusted rates(b) | 24.44 | 38.46 | 37.50 | 42.11 |
| Terminal rates(c) | 8/39(20.5) | 15/39(38.5) | 16/45(35.6) | 16/38(42.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.2906 | | | |
| Prevalence method(d) | P = 0.0690 | | | |
| Combined analysis(d) | P = 0.0580 | | | |
| Cochran-Armitage test(e) | P = 0.1250 | | | |
| Fisher Exact test(e) | | P = 0.2828 | P = 0.2828 | P = 0.0826 |
| SITE : pituitary gland TUMOR : adenoma,adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 15/49(30.6) | 18/50(36.0) | 18/50(36.0) | 22/50(44.0) |
| Adjusted rates(b) | 25.00 | 38.46 | 37.50 | 42.11 |
| Terminal rates(c) | 8/39(20.5) | 15/39(38.5) | 16/45(35.6) | 16/38(42.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.4357 | | | |
| Prevalence method(d) | P = 0.0770 | | | |
| Combined analysis(d) | P = 0.0899 | | | |
| Cochran-Armitage test(e) | P = 0.1755 | | | |
| Fisher Exact test(e) | | P = 0.3614 | P = 0.3614 | P = 0.1211 |

STUDY No. : 0318
ANIMAL : RAT F344/DuGrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|--------------|--------------|--------------|-------------|
| SITE : thyroid TUMOR : C-cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50(16.0) | 10/49(20.4) | 10/50(20.0) | 5/50(10.0) |
| Adjusted rates(b) | 16.33 | 23.26 | 21.74 | 13.16 |
| Terminal rates(c) | 6/39(15.4) | 9/39(23.1) | 9/45(20.0) | 5/38(13.2) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.8228 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.3111 | | | |
| Fisher Exact test(e) | | P = 0.3792 | P = 0.3976 | P = 0.2768 |
| SITE : thyroid TUMOR : follicular adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 3/49(6.1) | 0/50(0.0) | 1/50(2.0) |
| Adjusted rates(b) | 2.56 | 7.69 | 0.0 | 2.63 |
| Terminal rates(c) | 1/39(2.6) | 3/39(7.7) | 0/45(0.0) | 1/38(2.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.6906 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.5887 | | | |
| Fisher Exact test(e) | | P = 0.3010 | P = 0.5000 | P = 0.2475 |
| SITE : thyroid TUMOR : C-cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 0/49(0.0) | 1/50(2.0) | 0/50(0.0) |
| Adjusted rates(b) | 4.65 | 0.0 | 2.22 | 0.0 |
| Terminal rates(c) | 1/39(2.6) | 0/39(0.0) | 1/45(2.2) | 0/38(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9116 ? | | | |
| Prevalence method(d) | P = 0.8982 | | | |
| Combined analysis(d) | P = 0.9645 | | | |
| Cochran-Armitage test(e) | P = 0.0874 | | | |
| Fisher Exact test(e) | | P = 0.1250 | P = 0.3087 | P = 0.1212 |

STUDY No. : 0318
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|--------------|--------------|--------------|-------------|
| SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 11/50(22.0) | 10/49(20.4) | 11/50(22.0) | 5/50(10.0) |
| Adjusted rates(b) | 20.83 | 23.26 | 23.91 | 13.16 |
| Terminal rates(c) | 7/39(17.9) | 9/39(23.1) | 10/45(22.2) | 5/38(13.2) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9116 ? | | | |
| Prevalence method(d) | P = 0.9109 | | | |
| Combined analysis(d) | P = 0.9388 | | | |
| Cochran-Armitage test(e) | P = 0.1130 | | | |
| Fisher Exact test(e) | | P = 0.4791 | P = 0.4048 | P = 0.0857 |
| SITE : thyroid TUMOR : follicular adenoma,follicular adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 4/49(8.2) | 0/50(0.0) | 1/50(2.0) |
| Adjusted rates(b) | 2.56 | 9.09 | 0.0 | 2.63 |
| Terminal rates(c) | 1/39(2.6) | 3/39(7.7) | 0/45(0.0) | 1/38(2.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ——— | | | |
| Prevalence method(d) | P = 0.7437 | | | |
| Combined analysis(d) | P = ——— | | | |
| Cochran-Armitage test(e) | P = 0.4804 | | | |
| Fisher Exact test(e) | | P = 0.1748 | P = 0.5000 | P = 0.2475 |
| SITE : adrenal gland TUMOR : pheochromocytoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50(10.0) | 6/50(12.0) | 3/50(6.0) | 2/50(4.0) |
| Adjusted rates(b) | 12.20 | 15.00 | 6.52 | 5.26 |
| Terminal rates(c) | 4/39(10.3) | 5/39(12.8) | 2/45(4.4) | 2/38(5.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ——— | | | |
| Prevalence method(d) | P = 0.9152 | | | |
| Combined analysis(d) | P = ——— | | | |
| Cochran-Armitage test(e) | P = 0.1586 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.3575 | P = 0.2180 |

STUDY No. : 0318
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|---|--------------|--------------|--------------|--------------|
| SITE : adrenal gland TUMOR : pheochromocytoma,pheochromocytoma:malignant | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 6/50(12.0) | 4/50(8.0) | 3/50(6.0) |
| Adjusted rates(b) | 14.63 | 15.00 | 8.70 | 5.26 |
| Terminal rates(c) | 5/39(12.8) | 5/39(12.8) | 3/45(6.7) | 2/38(5.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1023 | | | |
| Prevalence method(d) | P = 0.9408 | | | |
| Combined analysis(d) | P = 0.8683 | | | |
| Cochran-Armitage test(e) | P = 0.2372 | | | |
| Fisher Exact test(e) | | P = 0.3798 | P = 0.3703 | P = 0.2435 |
| SITE : testis TUMOR : interstitial cell tumor | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 41/50(82.0) | 42/50(84.0) | 42/50(84.0) | 37/50(74.0) |
| Adjusted rates(b) | 97.44 | 92.50 | 85.11 | 82.50 |
| Terminal rates(c) | 38/39(97.4) | 36/39(92.3) | 38/45(84.4) | 31/38(81.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.8489 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.2470 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.2348 |

(HPT360A)

BAIS3

STUDY No. : 0318
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|---|------------|------------|------------|------------|
| SITE : peritoneum TUMOR : mesothelioma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 3/50(6.0) | 1/50(2.0) | 1/50(2.0) |
| Adjusted rates(b) | 0.0 | 5.13 | 2.22 | 2.50 |
| Terminal rates(c) | 0/39(0.0) | 2/39(5.1) | 1/45(2.2) | 0/38(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5841 | | | |
| Prevalence method(d) | P = 0.3511 | | | |
| Combined analysis(d) | P = 0.4474 | | | |
| Cochran-Armitage test(e) | P = 0.9390 | | | |
| Fisher Exact test(e) | | P = 0.1212 | P = 0.5000 | P = 0.5000 |

(HPT360A)

BAIS3

- (a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
—— : There is no data which should be statistical analysis.
Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

APPENDIX M 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANALYSIS, RAT: FEMALE

(2-YEAR STUDY)

STUDY No. : 0318
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : subcutis TUMOR : fibroma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 3/50(6.0) | 1/50(2.0) | 2/50(4.0) |
| Adjusted rates(b) | 0.0 | 5.26 | 2.50 | 5.00 |
| Terminal rates(c) | 0/39(0.0) | 2/38(5.3) | 1/40(2.5) | 2/40(5.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5999 | | | |
| Prevalence method(d) | P = 0.1741 | | | |
| Combined analysis(d) | P = 0.2570 | | | |
| Cochran-Armitage test(e) | P = 0.4835 | | | |
| Fisher Exact test(e) | | P = 0.1212 | P = 0.5000 | P = 0.2475 |
| SITE : spleen TUMOR : mononuclear cell leukemia | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50(10.0) | 9/50(18.0) | 3/50(6.0) | 4/50(8.0) |
| Adjusted rates(b) | 2.56 | 13.16 | 5.00 | 2.38 |
| Terminal rates(c) | 1/39(2.6) | 5/38(13.2) | 2/40(5.0) | 0/40(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7447 | | | |
| Prevalence method(d) | P = 0.7549 | | | |
| Combined analysis(d) | P = 0.8343 | | | |
| Cochran-Armitage test(e) | P = 0.3699 | | | |
| Fisher Exact test(e) | | P = 0.1940 | P = 0.3575 | P = 0.5000 |
| SITE : pituitary gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 18/50(36.0) | 20/50(40.0) | 18/50(36.0) | 18/50(36.0) |
| Adjusted rates(b) | 35.90 | 45.00 | 32.61 | 37.50 |
| Terminal rates(c) | 14/39(35.9) | 17/38(44.7) | 13/40(32.5) | 15/40(37.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.3925 | | | |
| Prevalence method(d) | P = 0.6527 | | | |
| Combined analysis(d) | P = 0.5936 | | | |
| Cochran-Armitage test(e) | P = 0.8819 | | | |
| Fisher Exact test(e) | | P = 0.4185 | P = 0.4176 | P = 0.4176 |

STUDY No. : 0318
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 8

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : pituitary gland TUMOR : adenoma,adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 18/50(36.0) | 21/50(42.0) | 20/50(40.0) | 19/50(38.0) |
| Adjusted rates(b) | 35.90 | 45.00 | 35.00 | 40.00 |
| Terminal rates(c) | 14/39(35.9) | 17/38(44.7) | 14/40(35.0) | 16/40(40.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.4442 | | | |
| Prevalence method(d) | P = 0.5551 | | | |
| Combined analysis(d) | P = 0.5251 | | | |
| Cochran-Armitage test(e) | P = 0.9609 | | | |
| Fisher Exact test(e) | | P = 0.3410 | P = 0.4185 | P = 0.5000 |
| SITE : thyroid TUMOR : C-cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50(16.0) | 6/50(12.0) | 2/50(4.0) | 5/50(10.0) |
| Adjusted rates(b) | 17.95 | 15.38 | 5.00 | 11.80 |
| Terminal rates(c) | 7/39(17.9) | 5/38(13.2) | 2/40(5.0) | 4/40(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.8751 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.2925 | | | |
| Fisher Exact test(e) | | P = 0.3871 | P = 0.0458* | P = 0.2768 |
| SITE : adrenal gland TUMOR : pheochromocytoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 4/50(8.0) | 0/50(0.0) | 1/50(2.0) |
| Adjusted rates(b) | 2.56 | 10.53 | 0.0 | 2.50 |
| Terminal rates(c) | 1/39(2.6) | 4/38(10.5) | 0/40(0.0) | 1/40(2.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.7584 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.4835 | | | |
| Fisher Exact test(e) | | P = 0.1811 | P = 0.5000 | P = 0.2475 |

STUDY No. : 0318
 ANIMAL : RAT F344/DuCrj
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 9

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|--------------|-------------|-------------|-------------|
| SITE : uterus TUMOR : endometrial stromal polyp | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 7/50(14.0) | 6/50(12.0) | 4/50(8.0) |
| Adjusted rates(b) | 13.64 | 15.00 | 15.00 | 8.33 |
| Terminal rates(c) | 5/39(12.8) | 5/38(13.2) | 6/40(15.0) | 2/40(5.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5977 | | | |
| Prevalence method(d) | P = 0.7737 | | | |
| Combined analysis(d) | P = 0.8029 | | | |
| Cochran-Armitage test(e) | P = 0.4314 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.3798 | P = 0.3703 |
| SITE : mammary gland TUMOR : fibroadenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 5/50(10.0) | 3/50(6.0) | 5/50(10.0) |
| Adjusted rates(b) | 12.82 | 13.16 | 6.67 | 11.86 |
| Terminal rates(c) | 5/39(12.8) | 5/38(13.2) | 2/40(5.0) | 3/40(7.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9183 ? | | | |
| Prevalence method(d) | P = 0.5966 | | | |
| Combined analysis(d) | P = 0.6998 | | | |
| Cochran-Armitage test(e) | P = 0.7137 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.2435 | P = 0.5000 |

(HPT360A)

BAIS3

STUDY No. : 0318
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 10

| Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--|------------|------------|------------|------------|
| SITE : preputial/clitoral gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 2/50(4.0) | 0/50(0.0) | 1/50(2.0) |
| Adjusted rates(b) | 7.69 | 0.0 | 0.0 | 2.50 |
| Terminal rates(c) | 3/39(7.7) | 0/38(0.0) | 0/40(0.0) | 1/40(2.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7428 | | | |
| Prevalence method(d) | P = 0.8465 | | | |
| Combined analysis(d) | P = 0.9028 | | | |
| Cochran-Armitage test(e) | P = 0.2072 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.1212 | P = 0.3087 |

(HPT360A)

BAIS3

- (a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
_____ : There is no data which should be statistical analysis.
Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

APPENDIX N 1

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: MALE: ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | 0ppm 50 | 3ppm 50 | 6ppm 50 | 12ppm 50 |
|---|----------------------------|---------------------------------------|------------|------------|------------|-------------|
| {Integumentary system/appandage} | | | | | | |
| subcutis | metastasis:thyroid tumor | | <50> 1 | <50> 0 | <50> 0 | <50> 0 |
| {Respiratory system} | | | | | | |
| nasal cavit | leukemic cell infiltration | | <50> 0 | <50> 2 | <50> 1 | <50> 0 |
| larynx | leukemic cell infiltration | | <50> 1 | <49> 0 | <50> 0 | <50> 0 |
| trachea | leukemic cell infiltration | | <50> 1 | <50> 0 | <50> 0 | <50> 0 |
| lung | leukemic cell infiltration | | <50> 2 | <50> 5 | <50> 3 | <50> 4 |
| | metastasis:adrenal tumor | | 0 | 0 | 0 | 1 |
| | metastasis:thyroid tumor | | 2 | 0 | 1 | 0 |
| | metastasis:subcutis tumor | | 1 | 0 | 0 | 0 |
| {Hematopoietic system} | | | | | | |
| bone marrow | leukemic cell infiltration | | <50> 1 | <50> 3 | <50> 2 | <50> 2 |
| | metastasis:liver tumor | | 0 | 1 | 0 | 0 |
| lymph node | leukemic cell infiltration | | <50> 2 | <50> 1 | <50> 2 | <50> 2 |
| | metastasis:liver tumor | | 0 | 1 | 0 | 0 |
| < a > a : Number of animals examined at the site b b : Number of animals with lesion | | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 2

| | | Group Name | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|------------------------|--|-------------------------|-----------|--|-----------|--|-----------|--|-----------|--|
| Organ | Findings | No. of Animals on Study | 50 | | 50 | | 50 | | 50 | |
| | | | | | | | | | | |
| {Hematopoietic system} | | | | | | | | | | |
| thymus | leukemic cell infiltration | | <50> 1 | | <50> 0 | | <50> 0 | | <50> 0 | |
| spleen | metastasis:liver tumor | | <50> 0 | | <50> 1 | | <50> 0 | | <50> 0 | |
| | | | | | | | | | | |
| {Circulatory system} | | | | | | | | | | |
| heart | leukemic cell infiltration | | <50> 0 | | <50> 1 | | <50> 1 | | <50> 2 | |
| | | | | | | | | | | |
| {Digestive system} | | | | | | | | | | |
| tongue | leukemic cell infiltration | | <50> 1 | | <50> 1 | | <50> 0 | | <50> 0 | |
| salivary gl | leukemic cell infiltration | | <50> 1 | | <50> 1 | | <50> 0 | | <50> 1 | |
| stomach | leukemic cell infiltration | | <50> 1 | | <50> 2 | | <50> 0 | | <50> 1 | |
| small intes | leukemic cell infiltration | | <50> 1 | | <50> 2 | | <50> 1 | | <50> 0 | |
| large intes | leukemic cell infiltration | | <50> 1 | | <50> 2 | | <50> 0 | | <50> 0 | |
| liver | leukemic cell infiltration | | <50> 2 | | <50> 5 | | <50> 3 | | <50> 5 | |
| pancreas | leukemic cell infiltration | | <50> 1 | | <50> 1 | | <50> 3 | | <50> 2 | |
| | | | | | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | | | | | |
| b | b : Number of animals with lesion | | | | | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ | Findings | Group Name | 0ppm | | 3ppm | | 6ppm | | 12ppm | | |
|-----------------------|--|-------------------------|------|--|------|--|------|--|-------|--|--|
| | | No. of Animals on Study | 50 | | 50 | | 50 | | 50 | | |
| {Digestive system} | | | | | | | | | | | |
| pancreas | | | <50> | | <50> | | <50> | | <50> | | |
| | metastasis:liver tumor | | 0 | | 1 | | 0 | | 0 | | |
| {Urinary system} | | | | | | | | | | | |
| kidney | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 1 | | 4 | | 2 | | 2 | | |
| urin bladd | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 1 | | 0 | | 1 | | 0 | | |
| {Endocrine system} | | | | | | | | | | | |
| pituitary | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 2 | | 3 | | 1 | | 1 | | |
| thyroid | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 1 | | 1 | | 1 | | 1 | | |
| parathyroid | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 1 | | 0 | | 0 | | 1 | | |
| adrenal | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 2 | | 4 | | 2 | | 0 | | |
| {Reproductive system} | | | | | | | | | | | |
| testis | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 1 | | 1 | | 0 | | 0 | | |
| | metastasis:peritoneum tumor | | 0 | | 1 | | 0 | | 0 | | |
| epididymis | | | <50> | | <50> | | <50> | | <50> | | |
| | leukemic cell infiltration | | 0 | | 1 | | 0 | | 0 | | |
| < a > | a : Number of animals examined at the site | | | | | | | | | | |
| b | b : Number of animals with lesion | | | | | | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ | Findings | Group Name | 0ppm | | 3ppm | | 6ppm | | 12ppm | | |
|----------------------------------|--|-------------------------|------|--|------|------|------|--|-------|--|--|
| | | No. of Animals on Study | 50 | | 50 | | 50 | | 50 | | |
| {Reproductive system} | | | | | | | | | | | |
| semin ves | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 1 | | | 1 | | | 0 | | |
| prostate | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 1 | | | 1 | | | 0 | | |
| mammary gl | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 0 | | | 1 | | | 0 | | |
| {Nervous system} | | | | | | | | | | | |
| brain | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 0 | | | 3 | | | 2 | | |
| | metastasis:pituitary tumor | | 1 | | | 0 | | | 0 | | |
| spinal cord | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 0 | | | 2 | | | 2 | | |
| {Special sense organs/appendage} | | | | | | | | | | | |
| eye | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 0 | | | 2 | | | 0 | | |
| Harder gl | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 1 | | | 2 | | | 1 | | |
| {Musculoskeletal system} | | | | | | | | | | | |
| muscle | | | <50> | | | <50> | | | <50> | | |
| | leukemic cell infiltration | | 1 | | | 1 | | | 0 | | |
| < a > | a : Number of animals examined at the site | | | | | | | | | | |
| b | b : Number of animals with lesion | | | | | | | | | | |

APPENDIX N 2

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: MALE: DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 1

| Organ | Findings | Group Name | Oppm | | | |
|------------------------|----------------------------|-------------------------|------|------|------|-------|
| | | No. of Animals on Study | 11 | 11 | 5 | 12 |
| | | | | 3ppm | 6ppm | 12ppm |
| {Respiratory system} | | | | | | |
| nasal cavit | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 0 | 2 | 1 | 0 |
| larynx | | | <11> | <10> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| trachea | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| lung | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 3 | 2 | 3 |
| | metastasis:adrenal tumor | | 0 | 0 | 0 | 1 |
| | metastasis:thyroid tumor | | 1 | 0 | 0 | 0 |
| {Hematopoietic system} | | | | | | |
| bone marrow | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 3 | 1 | 2 |
| | metastasis:liver tumor | | 0 | 1 | 0 | 0 |
| lymph node | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 1 | 1 | 2 |
| | metastasis:liver tumor | | 0 | 1 | 0 | 0 |
| thymus | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| spleen | | | <11> | <11> | < 5> | <12> |
| | metastasis:liver tumor | | 0 | 1 | 0 | 0 |
| {Circulatory system} | | | | | | |
| heart | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 2 |

< a > a : Number of animals examined at the site
 b b : Number of animals with lesion

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 2

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--------------------|--|-------------------------|------|------|------|-------|
| Organ | Findings | No. of Animals on Study | 11 | 11 | 5 | 12 |
| {Digestive system} | | | | | | |
| tongue | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 1 | 0 | 0 |
| salivary gl | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 1 | 0 | 1 |
| stomach | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 2 | 0 | 1 |
| small intes | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 2 | 0 | 0 |
| large intes | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 2 | 0 | 0 |
| liver | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 3 | 2 | 4 |
| pancreas | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 1 | 2 | 2 |
| | metastasis:liver tumor | | 0 | 1 | 0 | 0 |
| {Urinary system} | | | | | | |
| kidney | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 3 | 1 | 2 |
| urin bladd | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 0 | 1 | 0 |
| {Endocrine system} | | | | | | |
| pituitary | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 2 | 1 | 1 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 3

| | | Group Name | Oppm | | 3ppm | | 6ppm | | 12ppm | |
|-----------------------|--|-------------------------|------|--|------|--|------|--|-------|--|
| Organ | Findings | No. of Animals on Study | 11 | | 11 | | 5 | | 12 | |
| {Endocrine system} | | | | | | | | | | |
| thyroid | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 1 | | 1 | | 0 | | 1 | |
| parathyroid | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 1 | | 0 | | 0 | | 1 | |
| adrenal | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 1 | | 3 | | 2 | | 0 | |
| {Reproductive system} | | | | | | | | | | |
| testis | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 1 | | 1 | | 0 | | 0 | |
| epididymis | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 0 | | 1 | | 0 | | 0 | |
| semin ves | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 1 | | 1 | | 0 | | 1 | |
| prostate | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 1 | | 1 | | 0 | | 0 | |
| mammary gl | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 0 | | 1 | | 0 | | 1 | |
| {Nervous system} | | | | | | | | | | |
| brain | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 0 | | 3 | | 2 | | 1 | |
| | metastasis:pituitary tumor | | 1 | | 0 | | 0 | | 0 | |
| spinal cord | | | <11> | | <11> | | < 5> | | <12> | |
| | leukemic cell infiltration | | 0 | | 2 | | 2 | | 0 | |
| < a > | a : Number of animals examined at the site | | | | | | | | | |
| b | b : Number of animals with lesion | | | | | | | | | |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrJ
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 4

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|----------------------------------|----------------------------|-------------------------|------|------|------|-------|
| Organ | Findings | No. of Animals on Study | 11 | 11 | 5 | 12 |
| {Special sense organs/appendage} | | | | | | |
| eye | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 0 | 2 | 0 | 0 |
| Harder gl | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 2 | 1 | 0 |
| {Musculoskeletal system} | | | | | | |
| muscle | | | <11> | <11> | < 5> | <12> |
| | leukemic cell infiltration | | 1 | 1 | 0 | 0 |

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

(JPT150)

BAIS3

APPENDIX N 3

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: MALE: SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | 0ppm | 3ppm | 45ppm | 12ppm |
|----------------------------------|----------------------------|---------------------------------------|-----------|-----------|-----------|-----------|
| {Integumentary system/appandage} | | | | | | |
| subcutis | metastasis:thyroid tumor | | <39> 1 | <39> 0 | <45> 0 | <38> 0 |
| {Respiratory system} | | | | | | |
| lung | leukemic cell infiltration | | <39> 1 | <39> 2 | <45> 1 | <38> 1 |
| | metastasis:thyroid tumor | | 1 | 0 | 1 | 0 |
| | metastasis:subcutis tumor | | 1 | 0 | 0 | 0 |
| {Hematopoietic system} | | | | | | |
| bone marrow | leukemic cell infiltration | | <39> 0 | <39> 0 | <45> 1 | <38> 0 |
| lymph node | leukemic cell infiltration | | <39> 1 | <39> 0 | <45> 1 | <38> 0 |
| {Digestive system} | | | | | | |
| small intes | leukemic cell infiltration | | <39> 0 | <39> 0 | <45> 1 | <38> 0 |
| liver | leukemic cell infiltration | | <39> 1 | <39> 2 | <45> 1 | <38> 1 |
| pancreas | leukemic cell infiltration | | <39> 0 | <39> 0 | <45> 1 | <38> 0 |
| {Urinary system} | | | | | | |
| kidney | leukemic cell infiltration | | <39> 0 | <39> 1 | <45> 1 | <38> 0 |

< a > a : Number of animals examined at the site
 b b : Number of animals with lesion

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 2

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|-----------------------|--|-------------------------|------|------|------|-------|
| Organ_____ | Findings_____ | No. of Animals on Study | 39 | 39 | 45 | 38 |
| <hr/> | | | | | | |
| {Endocrine system} | | | | | | |
| pituitary | | <39> | <39> | <45> | <38> | |
| | leukemic cell infiltration | 1 | 1 | 0 | 0 | |
| thyroid | | <39> | <39> | <45> | <38> | |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 | |
| adrenal | | <39> | <39> | <45> | <38> | |
| | leukemic cell infiltration | 1 | 1 | 0 | 0 | |
| {Reproductive system} | | | | | | |
| testis | | <39> | <39> | <45> | <38> | |
| | metastasis:peritoneum tumor | 0 | 1 | 0 | 0 | |
| <hr/> | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

(JPT150)

BAIS3

APPENDIX N 4

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: FEMALE: ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 5

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|----------------------------------|--|-------------------------|------|------|------|-------|
| Organ_____ | Findings_____ | No. of Animals on Study | 50 | 50 | 50 | 50 |
| | | | | | | |
| {Integumentary system/appandage} | | | | | | |
| skin/app | | | <50> | <50> | <50> | <50> |
| | metastasis:subcutis tumor | | 0 | 0 | 1 | 0 |
| {Respiratory system} | | | | | | |
| nasal cavit | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| lung | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 5 | 4 | 1 | 4 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| | metastasis:uterus tumor | | 1 | 0 | 0 | 1 |
| | metastasis:mammary gland tumor | | 0 | 1 | 0 | 0 |
| {Hematopoietic system} | | | | | | |
| bone marrow | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| lymph node | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 2 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| | metastasis:uterus tumor | | 1 | 0 | 0 | 0 |
| thymus | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 6

| | | Group Name | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|----------------------|--|-------------------------|------|--|------|--|------|--|-------|--|
| Organ_____ | Findings_____ | No. of Animals on Study | 50 | | 50 | | 50 | | 50 | |
| <hr/> | | | | | | | | | | |
| {Circulatory system} | | | | | | | | | | |
| heart | | | <50> | | <50> | | <50> | | <50> | |
| | leukemic cell infiltration | | 4 | | 2 | | 1 | | 0 | |
| | metastasis:liver tumor | | 0 | | 0 | | 1 | | 0 | |
| | metastasis:lung tumor | | 1 | | 0 | | 0 | | 0 | |
| {Digestive system} | | | | | | | | | | |
| large intes | | | <50> | | <50> | | <50> | | <50> | |
| | metastasis:uterus tumor | | 0 | | 0 | | 0 | | 1 | |
| liver | | | <50> | | <50> | | <50> | | <50> | |
| | leukemic cell infiltration | | 5 | | 9 | | 1 | | 4 | |
| | metastasis:brain tumor | | 0 | | 0 | | 0 | | 1 | |
| pancreas | | | <50> | | <50> | | <50> | | <50> | |
| | leukemic cell infiltration | | 0 | | 0 | | 0 | | 2 | |
| {Urinary system} | | | | | | | | | | |
| kidney | | | <50> | | <50> | | <50> | | <50> | |
| | leukemic cell infiltration | | 3 | | 1 | | 0 | | 1 | |
| | metastasis:liver tumor | | 0 | | 0 | | 1 | | 0 | |
| | metastasis:uterus tumor | | 1 | | 0 | | 0 | | 0 | |
| urin bladd | | | <50> | | <50> | | <50> | | <50> | |
| | leukemic cell infiltration | | 1 | | 0 | | 0 | | 0 | |
| {Endocrine system} | | | | | | | | | | |
| pituitary | | | <50> | | <50> | | <50> | | <50> | |
| | leukemic cell infiltration | | 1 | | 0 | | 0 | | 1 | |
| <hr/> | | | | | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | | | | | |
| b | b : Number of animals with lesion | | | | | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrJ
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 7

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|----------------------------------|--|-------------------------|------|------|------|-------|
| Organ | Findings | No. of Animals on Study | 50 | 50 | 50 | 50 |
| | | | | | | |
| {Endocrine system} | | | | | | |
| adrenal | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 2 | 0 | 3 |
| {Reproductive system} | | | | | | |
| ovary | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 1 | 0 | 1 |
| uterus | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 2 |
| {Nervous system} | | | | | | |
| brain | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 2 | 1 | 0 | 1 |
| | metastasis:pituitary tumor | | 0 | 1 | 2 | 1 |
| spinal cord | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 2 | 1 | 0 | 1 |
| {Special sense organs/appendage} | | | | | | |
| eye | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| {Musculoskeletal system} | | | | | | |
| muscle | | | <50> | <50> | <50> | <50> |
| | metastasis:subcutis tumor | | 0 | 0 | 1 | 0 |
| | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

APPENDIX N 5

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: FEMALE: DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrJ
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 5

| | | Group Name | 0ppm | | 3ppm | | 6ppm | | 12ppm | |
|------------------------|--|-------------------------|------|------|------|----|------|----|-------|-------|
| Organ | Findings | No. of Animals on Study | 11 | 12 | 10 | 10 | 10 | 10 | 10 | 12ppm |
| | | | | | | | | | | |
| {Respiratory system} | | | | | | | | | | |
| nasal cavit | | | <11> | <12> | | | <10> | | | <10> |
| | leukemic cell infiltration | | 0 | 1 | | | 0 | | | 0 |
| lung | | | <11> | <12> | | | <10> | | | <10> |
| | leukemic cell infiltration | | 4 | 3 | | | 1 | | | 4 |
| | metastasis:liver tumor | | 0 | 0 | | | 1 | | | 0 |
| | metastasis:uterus tumor | | 0 | 0 | | | 0 | | | 1 |
| | metastasis:mammary gland tumor | | 0 | 1 | | | 0 | | | 0 |
| | | | | | | | | | | |
| {Hematopoietic system} | | | | | | | | | | |
| bone marrow | | | <11> | <12> | | | <10> | | | <10> |
| | leukemic cell infiltration | | 0 | 0 | | | 0 | | | 1 |
| | metastasis:liver tumor | | 0 | 0 | | | 1 | | | 0 |
| lymph node | | | <11> | <12> | | | <10> | | | <10> |
| | leukemic cell infiltration | | 0 | 0 | | | 0 | | | 2 |
| | metastasis:liver tumor | | 0 | 0 | | | 1 | | | 0 |
| thymus | | | <11> | <12> | | | <10> | | | <10> |
| | leukemic cell infiltration | | 0 | 0 | | | 0 | | | 1 |
| | | | | | | | | | | |
| {Circulatory system} | | | | | | | | | | |
| heart | | | <11> | <12> | | | <10> | | | <10> |
| | leukemic cell infiltration | | 4 | 1 | | | 1 | | | 0 |
| | metastasis:liver tumor | | 0 | 0 | | | 1 | | | 0 |
| | | | | | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | | | | | |
| b | b : Number of animals with lesion | | | | | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 6

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|----------------------|--|-------------------------|-----------|-----------|-----------|-----------|
| Organ | Findings | No. of Animals on Study | 11 | 12 | 10 | 10 |
| {Circulatory system} | | | | | | |
| heart | metastasis:lung tumor | | <11> 1 | <12> 0 | <10> 0 | <10> 0 |
| {Digestive system} | | | | | | |
| large intes | metastasis:uterus tumor | | <11> 0 | <12> 0 | <10> 0 | <10> 1 |
| liver | leukemic cell infiltration | | <11> 4 | <12> 4 | <10> 1 | <10> 4 |
| | metastasis:brain tumor | | 0 | 0 | 0 | 1 |
| pancreas | leukemic cell infiltration | | <11> 0 | <12> 0 | <10> 0 | <10> 2 |
| {Urinary system} | | | | | | |
| kidney | leukemic cell infiltration | | <11> 3 | <12> 1 | <10> 0 | <10> 1 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| urin bladd | leukemic cell infiltration | | <11> 1 | <12> 0 | <10> 0 | <10> 0 |
| {Endocrine system} | | | | | | |
| pituitary | leukemic cell infiltration | | <11> 1 | <12> 0 | <10> 0 | <10> 1 |
| adrenal | leukemic cell infiltration | | <11> 1 | <12> 2 | <10> 0 | <10> 3 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 7

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|----------------------------------|--|-------------------------|-----------|-----------|-----------|-----------|
| Organ | Findings | No. of Animals on Study | 11 | 12 | 10 | 10 |
| {Reproductive system} | | | | | | |
| ovary | leukemic cell infiltration | | <11> 1 | <12> 1 | <10> 0 | <10> 1 |
| uterus | leukemic cell infiltration | | <11> 0 | <12> 0 | <10> 0 | <10> 2 |
| {Nervous system} | | | | | | |
| brain | leukemic cell infiltration | | <11> 2 | <12> 1 | <10> 0 | <10> 1 |
| | metastasis:pituitary tumor | | 0 | 1 | 1 | 0 |
| spinal cord | leukemic cell infiltration | | <11> 2 | <12> 1 | <10> 0 | <10> 1 |
| {Special sense organs/appendage} | | | | | | |
| eye | leukemic cell infiltration | | <11> 0 | <12> 1 | <10> 0 | <10> 0 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

APPENDIX N 6

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: FEMALE: SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0318
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 3

| Group Name | | 0ppm | 3ppm | 6ppm | 12ppm |
|--|----------------------------|-----------|-----------|-----------|-----------|
| No. of Animals on Study | | 39 | 38 | 40 | 40 |
| Organ | Findings | | | | |
| {Integumentary system/appandage} | | | | | |
| skin/app | metastasis:subcutis tumor | <39> 0 | <38> 0 | <40> 1 | <40> 0 |
| {Respiratory system} | | | | | |
| lung | leukemic cell infiltration | <39> 1 | <38> 1 | <40> 0 | <40> 0 |
| | metastasis:uterus tumor | 1 | 0 | 0 | 0 |
| {Hematopoietic system} | | | | | |
| lymph node | metastasis:uterus tumor | <39> 1 | <38> 0 | <40> 0 | <40> 0 |
| {Circulatory system} | | | | | |
| heart | leukemic cell infiltration | <39> 0 | <38> 1 | <40> 0 | <40> 0 |
| {Digestive system} | | | | | |
| liver | leukemic cell infiltration | <39> 1 | <38> 5 | <40> 0 | <40> 0 |
| {Urinary system} | | | | | |
| kidney | metastasis:uterus tumor | <39> 1 | <38> 0 | <40> 0 | <40> 0 |
| {Nervous system} | | | | | |
| brain | metastasis:pituitary tumor | <39> 0 | <38> 0 | <40> 1 | <40> 1 |
| < a > a : Number of animals examined at the site | | | | | |
| b b : Number of animals with lesion | | | | | |

STUDY NO. : 0318
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 4

| | | Group Name | 0ppm | 3ppm | 6ppm | 12ppm |
|--------------------------|--|-------------------------|------|------|------|-------|
| Organ | Findings | No. of Animals on Study | 39 | 38 | 40 | 40 |
| {Musculoskeletal system} | | | | | | |
| muscle | metastasis:subcutis tumor | | <39> | <38> | <40> | <40> |
| | | | 0 | 0 | 1 | 0 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

(JPT150)

BAIS3

APPENDIX O 1

IDENTITY AND IMPURITY OF CROTONALDEHYDE IN THE 2-YEAR INHALATION STUDY

IDENTITY AND IMPURITY OF CROTONALDEHYDE IN THE 2-YEAR INHALATION STUDY

Test Substance : Crotonaldehyde (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : SKJ4743

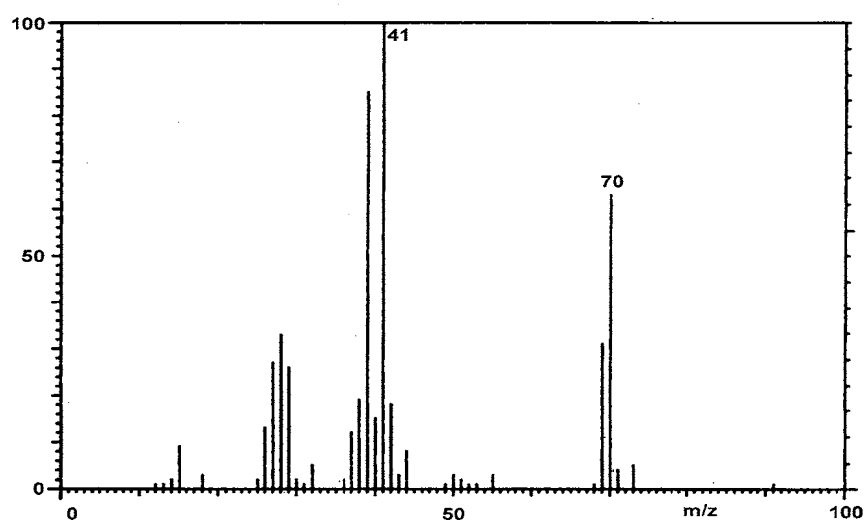
1. Spectral data

Mass Spectrometry

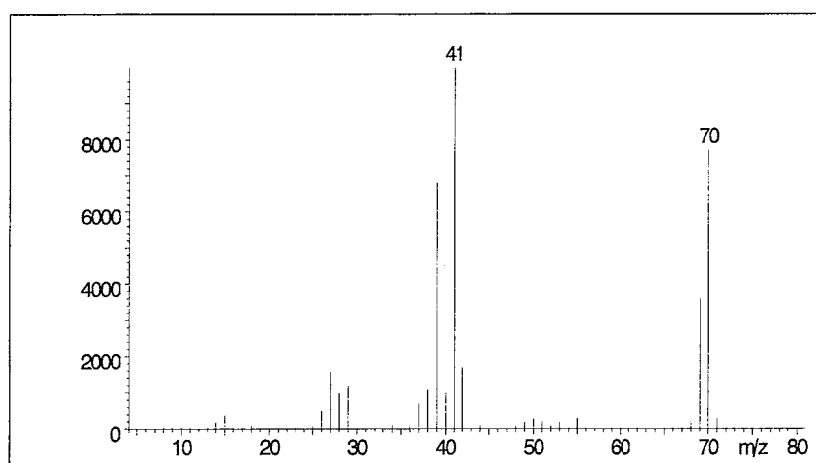
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

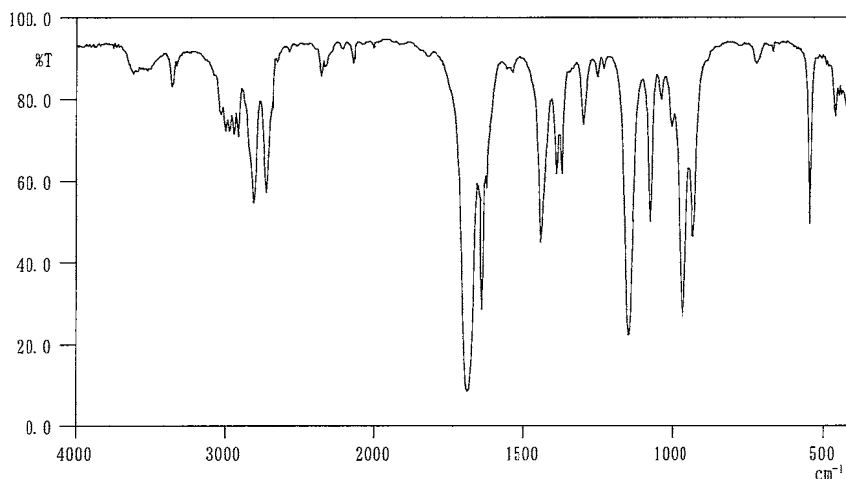
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.
John Wiley and Sons, Inc. (U.S.), Entry Number 1111)

Infrared Spectrometry

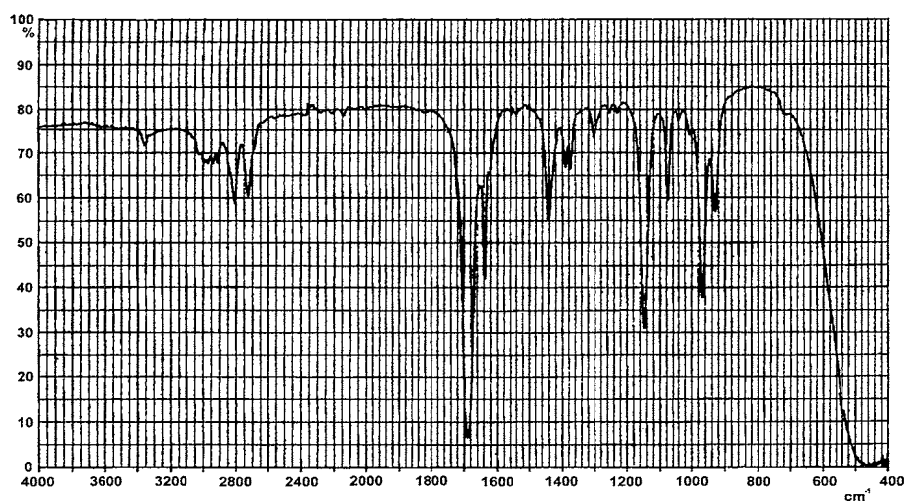
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.
(*Performed by the Wako Pure Chemical Industries, Ltd.)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : FALM (2 mm ϕ \times 2 m)
Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150° C
Flow Rate : 25 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|----------------|
| Test Substance | 1 | 99.89 | Crotonaldehyde |
| | 2 | 0.07 | N.I.M.* |
| | 3 | 0.04 | Crotonic Acid |

* Not Identified Material

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities.

It was identified only by comparing its gas chromatograph with that of crotonic acid (peak No.3) in the crotonaldehyde, the amounts in the test substance were 99.89% and 0.04%. However, peak No.2 cannot be identified, the amount of the peak was 0.07%.

3. Conclusions: The test substance was identified as crotonaldehyde, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (crotonaldehyde) and two impurities.

B. Lot No. : LEL4703

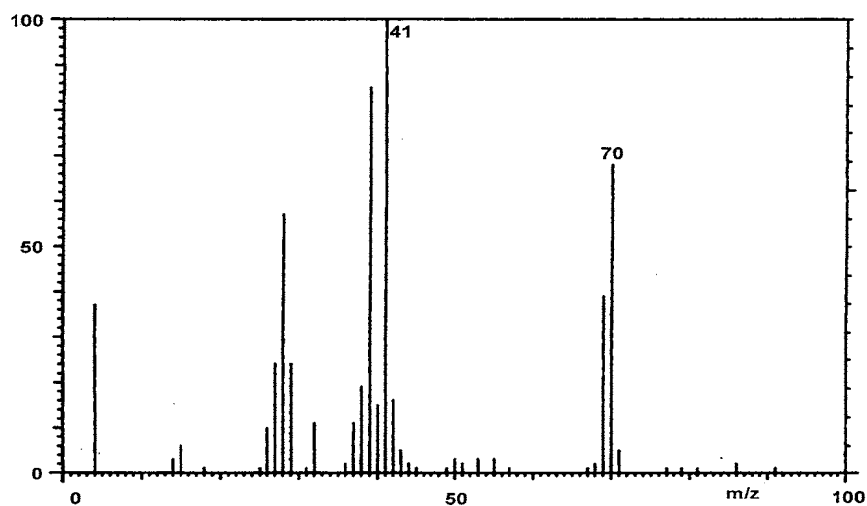
1. Spectral data

Mass Spectrometry

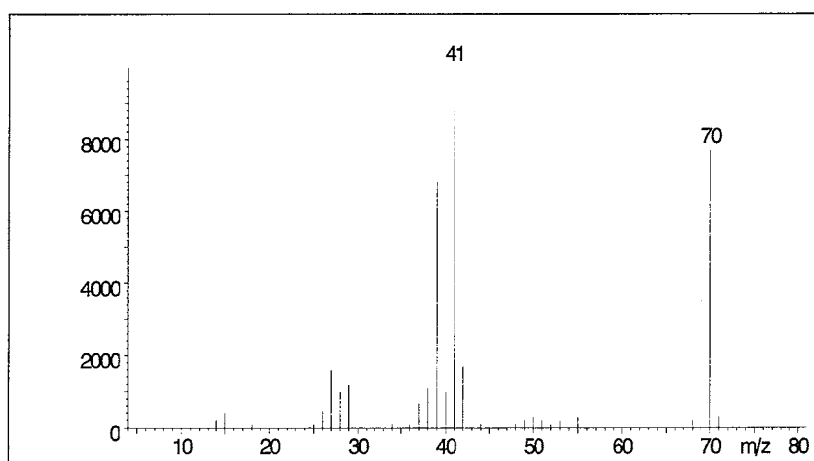
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

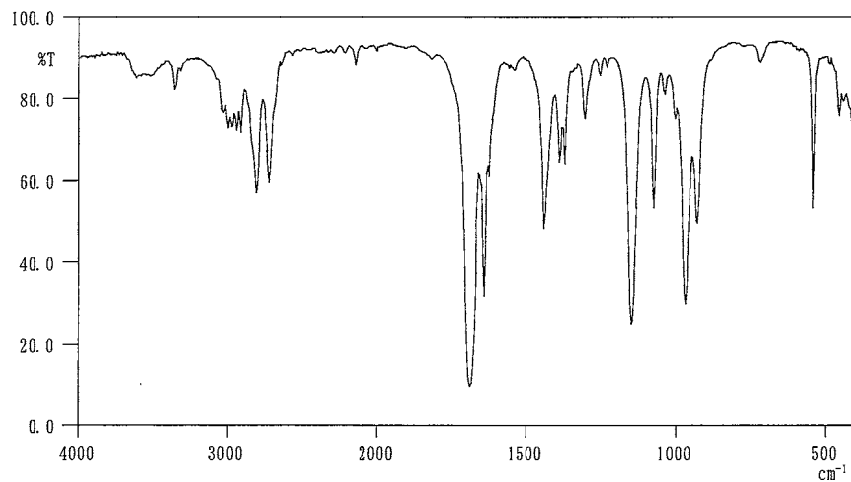
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.
John Wiley and Sons, Inc. (U.S.), Entry Number 1111)

Infrared Spectrometry

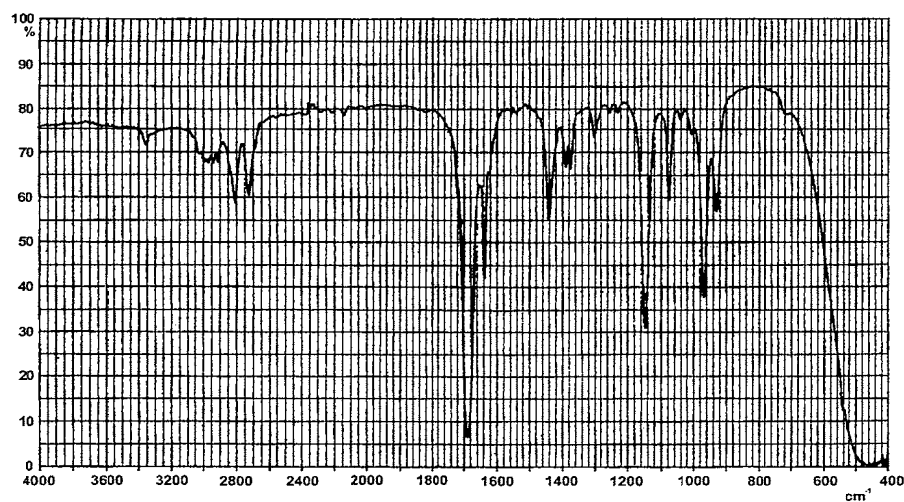
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.
(*Performed by the Wako Pure Chemical Industries, Ltd.)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : FALM (2 mm ϕ \times 2 m)
Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°
Flow Rate : 25 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|----------------|
| Test Substance | 1 | 99.86 | Crotonaldehyde |
| | 2 | 0.07 | N.I.M.* |
| | 3 | 0.07 | Crotonic Acid |

* Not Identified Material

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of crotonic acid (peak No.3) in the crotonaldehyde, the amounts in the test substance were 99.86% and 0.07%. However, peak No.2 cannot be identified, the amount of the peak was 0.07%.

3. Conclusions: The test substance was identified as crotonaldehyde, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (crotonaldehyde) and two impurities.

C. Lot No. : LEH5371

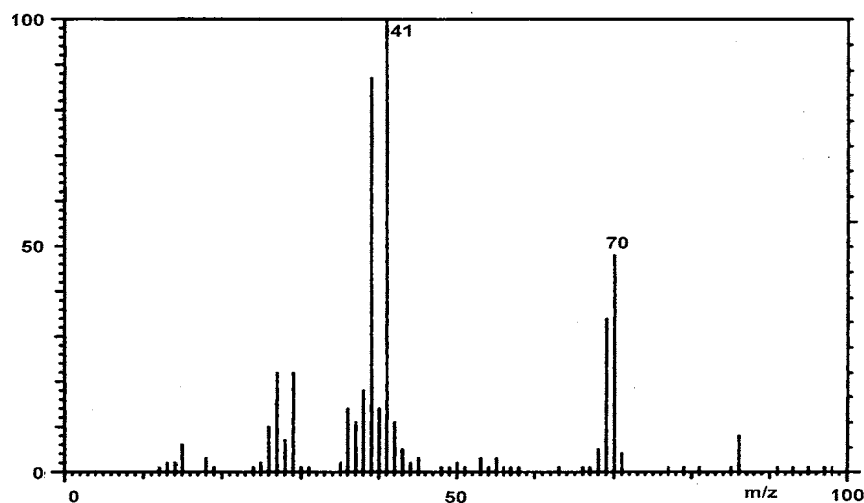
1. Spectral data

Mass Spectrometry

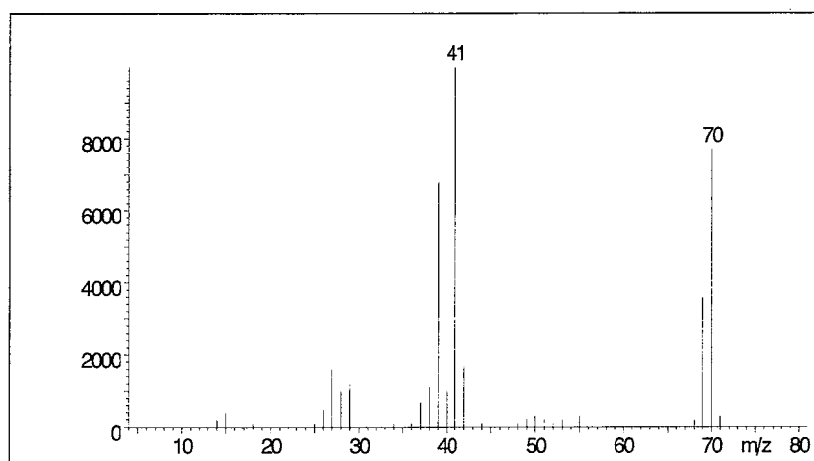
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

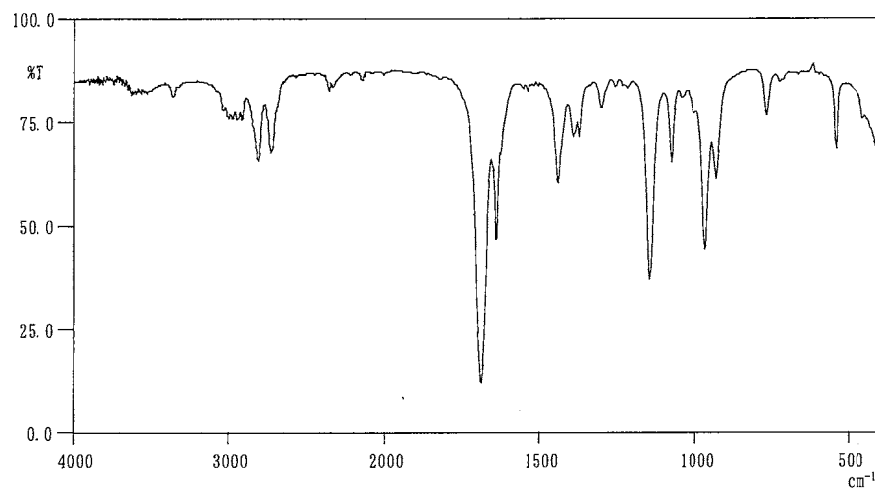
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.
John Wiley and Sons, Inc. (U.S.), Entry Number 1111)

Infrared Spectrometry

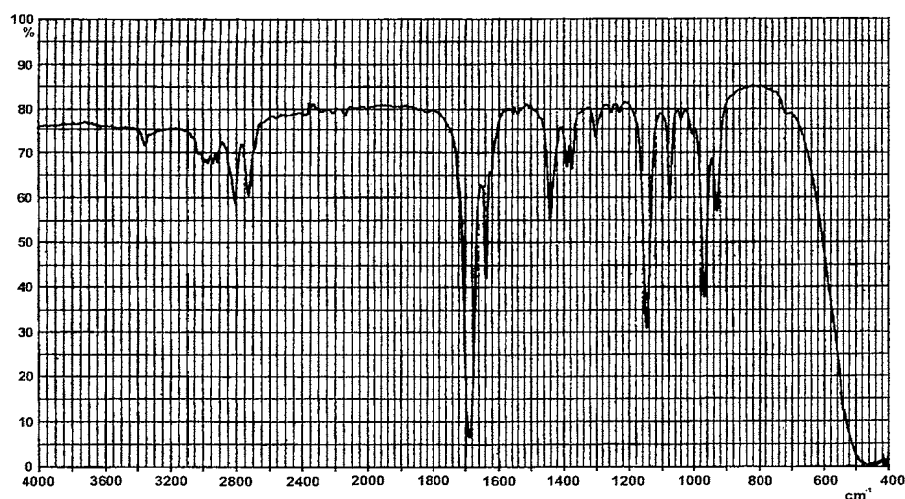
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.
(*Performed by the Wako Pure Chemical Industries, Ltd.)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : FALM (2 mm ϕ \times 2 m)
Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°
Flow Rate : 25 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|----------------|
| Test Substance | 1 | 99.86 | Crotonaldehyde |
| | 2 | 0.05 | N.I.M.* |
| | 3 | 0.09 | Crotonic Acid |

* Not Identified Material

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of crotonic acid (peak No.3) in the crotonaldehyde, the amounts in the test substance were 99.86% and 0.09%. However, peak No.2 cannot be identified, the amount of the peak was 0.05%.

3. Conclusions: The test substance was identified as crotonaldehyde, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (crotonaldehyde) and two impurities.

D. Lot No. : WTK5303

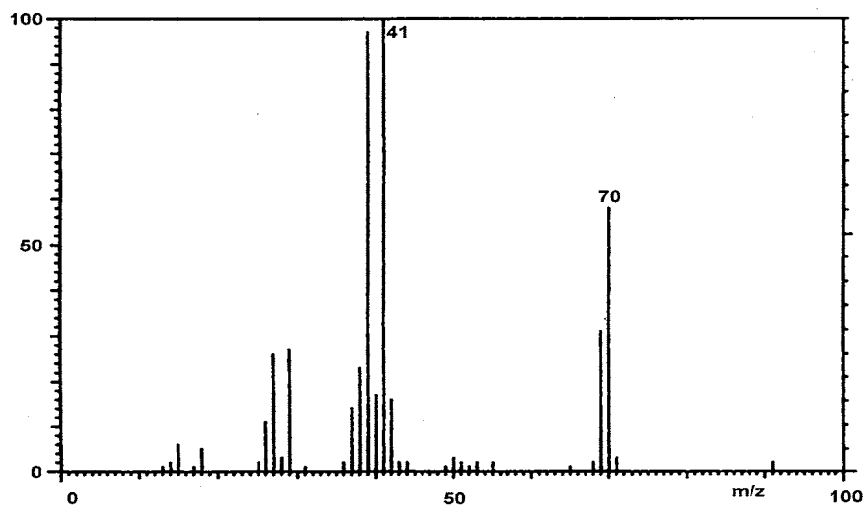
1. Spectral data

Mass Spectrometry

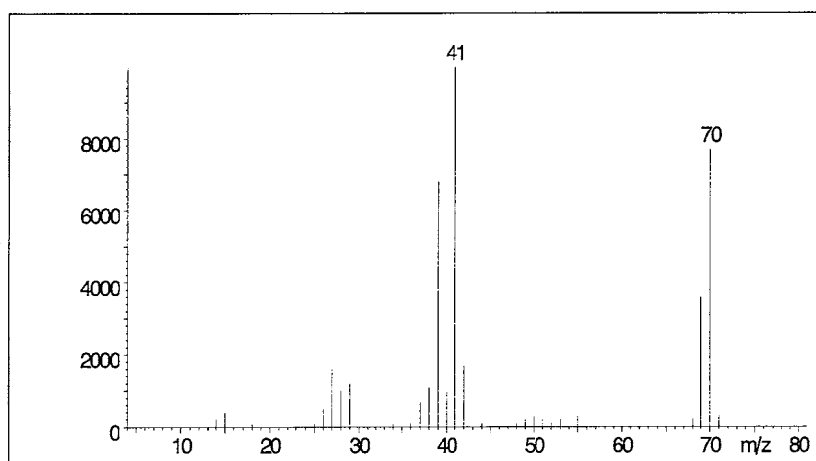
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

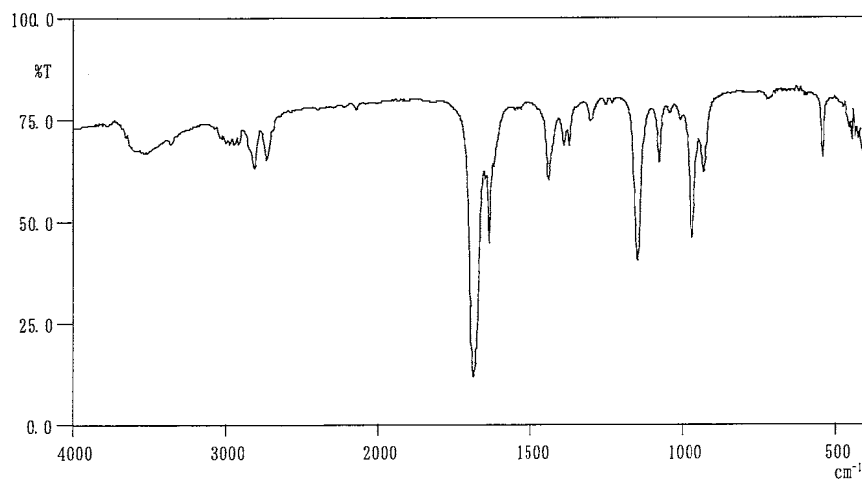
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.
John Wiley and Sons, Inc. (U.S.), Entry Number 1111)

Infrared Spectrometry

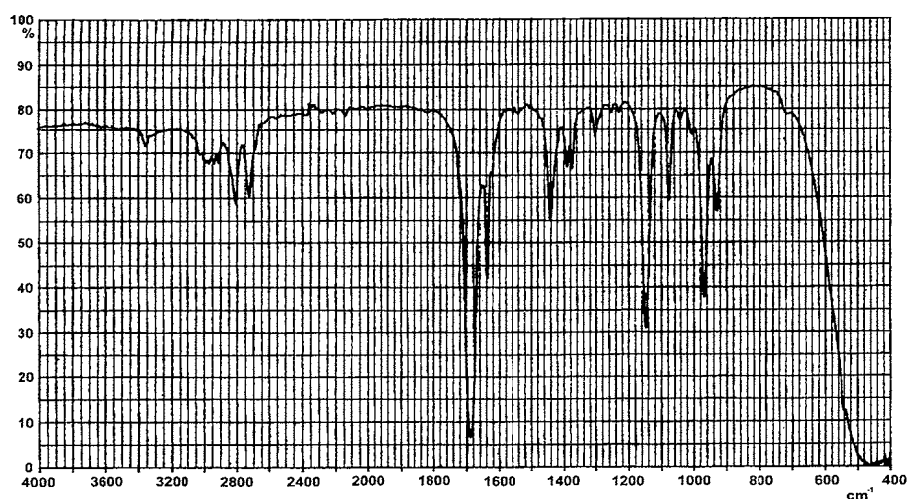
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.
(*Performed by the Wako Pure Chemical Industries, Ltd.)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : FALM (2 mm ϕ \times 2 m)
Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°
Flow Rate : 25 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|----------------|
| Test Substance | 1 | 99.85 | Crotonaldehyde |
| | 2 | 0.04 | N.I.M.* |
| | 3 | 0.11 | Crotonic Acid |

* Not Identified Material

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of crotonic acid (peak No.3) in the crotonaldehyde, the amounts in the test substance were 99.85% and 0.11%. However, peak No.2 cannot be identified, the amount of the peak was 0.04%.

3. Conclusions: The test substance was identified as crotonaldehyde, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (crotonaldehyde) and two impurities.

E. Lot No. : WTE4391

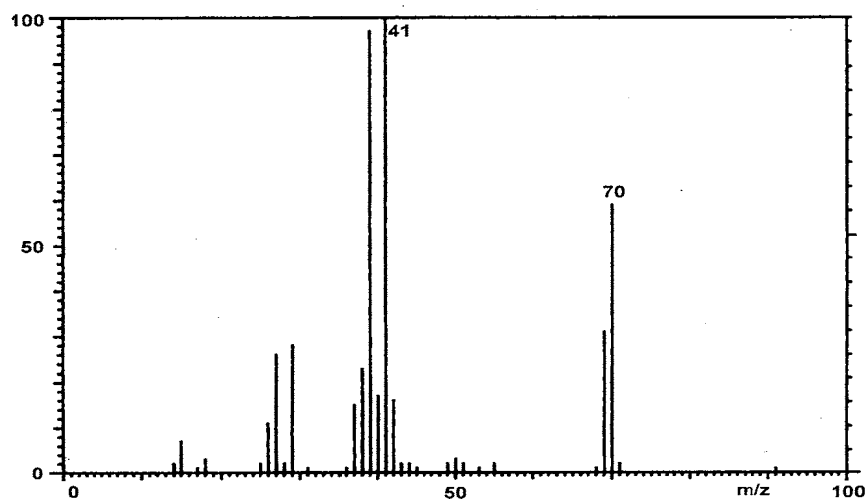
1. Spectral data

Mass Spectrometry

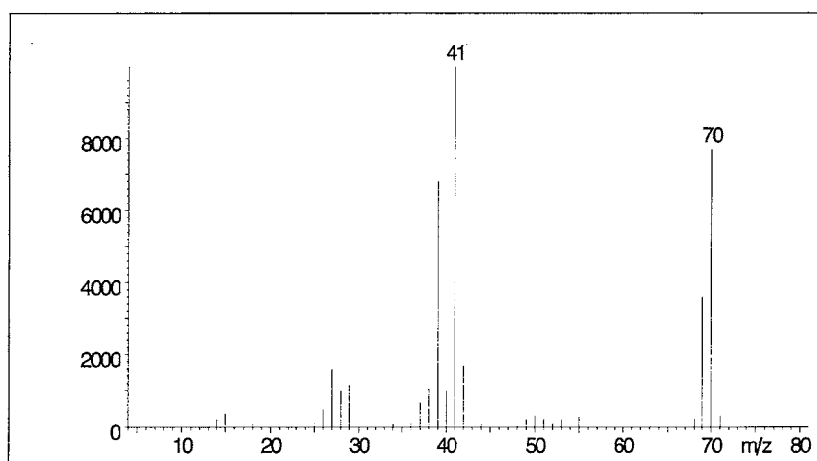
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

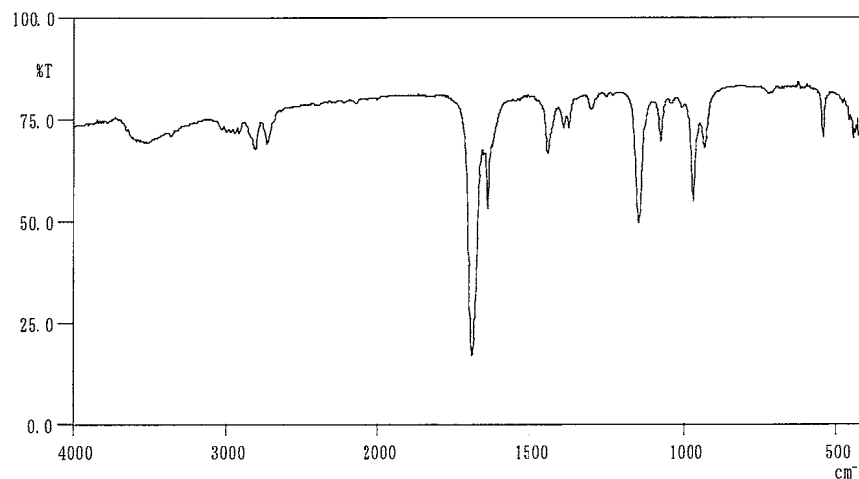
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.
John Wiley and Sons, Inc. (U.S.), Entry Number 1111)

Infrared Spectrometry

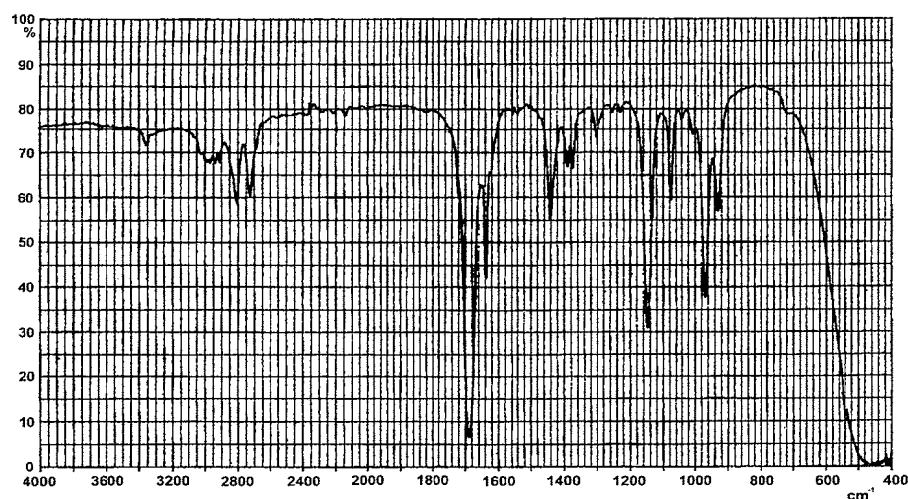
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.
(*Performed by the Wako Pure Chemical Industries, Ltd.)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : FALM (2 mm ϕ \times 2 m)
Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°
Flow Rate : 25 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|----------------|
| Test Substance | 1 | 99.85 | Crotonaldehyde |
| | 2 | 0.04 | N.I.M.* |
| | 3 | 0.11 | Crotonic Acid |

* Not Identified Material

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities.

It was identified only by comparing its gas chromatograph with that of crotonic acid (peak No.3) in the crotonaldehyde, the amounts in the test substance were 99.85% and 0.11%. However, peak No.2 cannot be identified, the amount of the peak was 0.04%.

3. Conclusions: The test substance was identified as crotonaldehyde, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (crotonaldehyde) and two impurities.

APPENDIX O 2
STABILITY OF CROTONALDEHYDE IN THE 2-YEAR
INHALATION STUDY

STABILITY OF CROTONALDEHYDE IN THE 2-YEAR INHALATION STUDY

Test Substance : Crotonaldehyde (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : SKJ4743

1. Sample : This lot was used from 1996.10.24 to 1997.4.1. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : FALM (2 mm ϕ \times 2 m)

Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°

Flow Rate : 25 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 1996.10.21 | 1 | 2.058 | 99.89 |
| | 2 | 4.828 | 0.07 |
| | 3 | 10.235 | 0.04 |
| 1997.04.03 | 1 | 2.048 | 99.88 |
| | 2 | 4.824 | 0.07 |
| | 3 | 10.224 | 0.05 |

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1996.10.21 and one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1997.4.3. No new trace impurity peak in the test substance analyzed at 1997.4.3 was detected.

3. Conclusions: The test substance was stable for about 6 months at room temperature.

B. Lot No. : LEL4703

1. Sample : This lot was used from 1997.4.2 to 1997.8.25. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : FALM (2 mm ϕ \times 2 m)

Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°

Flow Rate : 25 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 1997.04.01 | 1 | 2.056 | 99.86 |
| | 2 | 4.823 | 0.07 |
| | 3 | 10.219 | 0.07 |
| 1997.08.26 | 1 | 2.060 | 99.85 |
| | 2 | 4.822 | 0.07 |
| | 3 | 10.217 | 0.08 |

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1997.4.1 and one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1997.8.26. No new trace impurity peak in the test substance analyzed at 1997.8.26 was detected.

3. Conclusions: The test substance was stable for about 5 months at room temperature.

C. Lot No. : LEH5371

1. Sample : This lot was used from 1997.8.26 to 1998.1.6. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : FALM (2 mm ϕ \times 2 m)

Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°

Flow Rate : 25 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 1997.08.25 | 1 | 2.050 | 99.86 |
| | 2 | 4.821 | 0.05 |
| | 3 | 10.213 | 0.09 |
| 1998.01.07 | 1 | 2.057 | 99.90 |
| | 2 | 5.009 | 0.05 |
| | 3 | 10.329 | 0.05 |

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1997.8.25 and one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1998.1.7. No new trace impurity peak in the test substance analyzed at 1998.1.7 was detected.

3. Conclusions: The test substance was stable for about 5 months at room temperature.

D. Lot No. : WTK5303

1. Sample : This lot was used from 1998.1.7 to 1998.7.21. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : FALM (2 mm ϕ \times 2 m)

Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°

Flow Rate : 25 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 1998.01.05 | 1 | 2.059 | 99.85 |
| | 2 | 5.010 | 0.04 |
| | 3 | 10.300 | 0.11 |
| 1998.07.22 | 1 | 2.056 | 99.83 |
| | 2 | 5.007 | 0.05 |
| | 3 | 10.288 | 0.12 |

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1998.1.5 and one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1998.7.22. No new trace impurity peak in the test substance analyzed at 1998.7.22 was detected.

3. Conclusions: The test substance was stable for about 7 months at room temperature.

E. Lot No. : WTE4391

1. Sample : This lot was used from 1998.7.22 to 1998.10.21. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : FALM (2 mm ϕ \times 2 m)

Column Temperature: 60° C \rightarrow (10° C/min) \rightarrow 150°

Flow Rate : 25 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 1998.07.21 | 1 | 2.055 | 99.85 |
| | 2 | 5.005 | 0.04 |
| | 3 | 10.290 | 0.11 |
| 1998.11.30 | 1 | 2.053 | 99.81 |
| | 2 | 5.004 | 0.04 |
| | 3 | 10.274 | 0.15 |

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1998.7.21 and one major peak (peak No.1) and two impurities (peaks No.2 and 3 < 0.2% of total area) analyzed at 1998.11.30. No new trace impurity peak in the test substance analyzed at 1998.11.30 was detected.

3. Conclusions: The test substance was stable for about 6 months at room temperature.

APPENDIX P 1

CONCENTRATION OF CROTONALDEHYDE IN THE INHALATION CHAMBER
OF THE 2-YEAR INHALATION STUDY

CONCENTRATION OF CROTONALDEHYDE IN THE INHALATION CHAMBER
OF THE 2-YEAR INHALATION STUDY

| Group Name | Concentration (ppm) |
|------------|---------------------|
| | Mean \pm S.D. |
| 0 ppm | 0.0 \pm 0.0 |
| 3 ppm | 3.0 \pm 0.0 |
| 6 ppm | 6.0 \pm 0.0 |
| 12 ppm | 12.0 \pm 0.1 |

APPENDIX P 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER
IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

| Group Name | Temperature(°C) Mean ± S.D. | Humidity(%) Mean ± S.D. | Ventilation Rate(L/min) Mean ± S.D. | Air Changes(time/h) Mean |
|------------|--------------------------------|----------------------------|--|-----------------------------|
| 0 ppm | 22.1 ± 0.2 | 54.1 ± 1.8 | 1534.8 ± 28.7 | 12.1 |
| 3 ppm | 22.0 ± 0.1 | 53.7 ± 1.7 | 1534.2 ± 30.5 | 12.1 |
| 6 ppm | 22.4 ± 0.3 | 55.1 ± 1.9 | 1519.4 ± 27.1 | 12.0 |
| 12 ppm | 22.5 ± 0.3 | 53.2 ± 1.8 | 1530.7 ± 28.3 | 12.1 |

APPENDIX Q 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS
IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

| Item | Method |
|---|---|
| Hematology | |
| Red blood cell (RBC) | Light scattering method ¹⁾ |
| Hemoglobin (Hgb) | Cyanmethemoglobin method ¹⁾ |
| Hematocrit (Hct) | Calculated as $RBC \times MCV / 10$ ¹⁾ |
| Mean corpuscular volume (MCV) | Light scattering method ¹⁾ |
| Mean corpuscular hemoglobin (MCH) | Calculated as $Hgb / RBC \times 10$ ¹⁾ |
| Mean corpuscular hemoglobin concentration (MCHC) | Calculated as $Hgb / Hct \times 100$ ¹⁾ |
| Platelet | Light scattering method ¹⁾ |
| White blood cell (WBC) | Light scattering method ¹⁾ |
| Differential WBC | Pattern recognition method ²⁾ (Wright staining) |
| Biochemistry | |
| Total protein (TP) | Biuret method ³⁾ |
| Albumin (Alb) | BCG method ³⁾ |
| A/G ratio | Calculated as $Alb / (TP - Alb)$ ³⁾ |
| T-bilirubin | Alkaline azobilirubin method ³⁾ |
| Glucose | GlcK · G-6-PDH method ³⁾ |
| T-cholesterol | CE · COD · POD method ³⁾ |
| Triglyceride | LPL · GK · GPO · POD method ³⁾ |
| Phospholipid | PLD · ChOD · POD method ³⁾ |
| Glutamic oxaloacetic transaminase (GOT) | JSCC method ³⁾ |
| Glutamic pyruvic transaminase (GPT) | JSCC method ³⁾ |
| Lactate dehydrogenase (LDH) | SFBC method ³⁾ |
| Alkaline phosphatase (ALP) | GSCC method ³⁾ |
| γ -Glutamyl transpeptidase (γ -GTP) | L- γ -Glutamyl-p-nitroanilide method ³⁾ |
| Creatine phosphokinase (CPK) | JSCC method ³⁾ |
| Urea nitrogen | Urease · GLDH method ³⁾ |
| Creatinine | Jaffe method ³⁾ |
| Sodium | Ion selective electrode method ³⁾ |
| Potassium | Ion selective electrode method ³⁾ |
| Chloride | Ion selective electrode method ³⁾ |
| Calcium | OCPC method ³⁾ |
| Inorganic phosphorus | PNP · XOD · POD method ³⁾ |
| Urinalysis | |
| pH, Protein, Glucose, Ketone body, Bilirubin, Occult blood, Urobilinogen | Urinalysis reagent paper method ⁴⁾ |

1) Automatic blood cell analyzer (Technicon H·1 : Bayer Corporation)

2) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)

3) Automatic analyzer (Hitachi 7070 : Hitachi, Ltd.)

4) Ames reagent strips for urinalysis (Uro-Labstix : Bayer Corporation)

APPENDIX Q 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

| Item | Unit | Decimal place |
|--|-----------------------------|---------------|
| Hematology | | |
| Red blood cell (RBC) | $\times 10^6 / \mu\text{L}$ | 2 |
| Hemoglobin | g/dL | 1 |
| Hematocrit | % | 1 |
| Mean corpuscular volume (MCV) | fL | 1 |
| Mean corpuscular hemoglobin (MCH) | pg | 1 |
| Mean corpuscular hemoglobin concentration (MCHC) | g/dL | 1 |
| Platelet | $\times 10^3 / \mu\text{L}$ | 0 |
| White blood cell (WBC) | $\times 10^3 / \mu\text{L}$ | 2 |
| Differential WBC | % | 0 |
| Biochemistry | | |
| Total protein | g/dL | 1 |
| Albumin | g/dL | 1 |
| A/G ratio | — | 1 |
| T-bilirubin | mg/dL | 2 |
| Glucose | mg/dL | 0 |
| T-cholesterol | mg/dL | 0 |
| Triglyceride | mg/dL | 0 |
| Phospholipid | mg/dL | 0 |
| Glutamic oxaloacetic transaminase (GOT) | IU/L | 0 |
| Glutamic pyruvic transaminase (GPT) | IU/L | 0 |
| Lactate dehydrogenase (LDH) | IU/L | 0 |
| Alkaline phosphatase (ALP) | IU/L | 0 |
| γ -Glutamyl transpeptidase (γ -GTP) | IU/L | 0 |
| Creatine phosphokinase (CPK) | IU/L | 0 |
| Urea nitrogen | mg/dL | 1 |
| Creatinine | mg/dL | 1 |
| Sodium | mEq/L | 0 |
| Potassium | mEq/L | 1 |
| Chloride | mEq/L | 0 |
| Calcium | mg/dL | 1 |
| Inorganic phosphorus | mg/dL | 1 |